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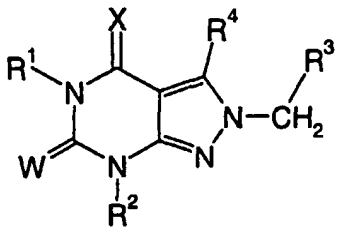
(54) Title: PYRAZOLO [3,4-d] PYRIMIDINE DERIVATIVES AND THEIR USE IN THE TREATMENT OF H.PYLORI INFECTION



(I)

(57) Abstract: This invention relates to novel compounds having the structural diagram (I) and to their pharmaceutical compositions and to their methods of use. These novel compounds provide a treatment or prophylaxis of *H. pylori* infection.

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Pyrazolo [3,4-d] pyrimidine derivates and their use in the treatment of H.pylori infection.

## Field of the invention

The present invention relates to novel fused heterocycles, their pharmaceutical compositions and methods of use. In addition, the present invention relates to therapeutic methods for the treatment and prevention of various diseases caused by *Helicobacter pylori* (*H. pylori)* infection.

## Background of the invention

*Helicobacter pylori* (*H. pylori*) is a highly motile, S-shaped, microaerophilic gram-negative bacterium that colonizes in the stomach. *H. pylori* infection is widespread with seroprevalence in the developed world between 30-60%. Infection with the bacterium is usually contracted during childhood and patients remain infected for life unless treated. *H. pylori* infection has been shown to result in the development of gastritis, peptic ulcer, and mucosa-associated lymphoid tissue (MALT) lymphoma and has been linked to gastric adenocarcinoma (Go, M.F. and D.T. Smoot, *Helicobacter pylori,* gastric MALT lymphoma, and adenocarcinoma of the stomach. Seminars in Gastrointestinal Disease, 2000, 11(3): p. 134-141). Eradication of *H. pylori* infection is currently achieved using combination therapy of antimicrobial and antisecretory agents (Malfertheiner, P., A. Leodolter, and U. Peitz, Cure of *Helicobacter pylori*-associated ulcer disease through eradication. Bailliere's Best Practice and Research in Clinical Gastroenterology, 2000, 14(1): p. 119-132). However, compliance to these therapies is compromised due to adverse side effects and cumbersome dosing regimens. In addition, increasing prevalence of *H. pylori* strains resistant to existing antimicrobial therapies threatens to limit the use of these treatments (Qureshi, W.A. and D.Y. Graham, *Antibiotic-resistant H. pylori infection and its treatment.* Current Pharmaceutical Design, 2000, 6(15): p. 1537-1544). Given these considerations, an ideal therapy for *H. pylori* infection would be a novel antimicrobial monotherapy that is selective for *H. pylori* eradication. The selectivity attribute is expected to aid in minimizing side effects due effects on gut flora.

*H. pylori*, like all Gram positive and Gram negative bacteria, utilize a cell wall comprised of crosslinked peptidoglycan units to maintain shape and resist high osmotic pressure potentials. Bacterial cell wall biosynthesis is a validated target for antimicrobial activity; cephalosphorins, penicillins and glycopeptides are antimicrobial agents, which block cell wall biosynthesis (Walsh, C., *Molecular mechanisms that confer antibacterial resistance.* Nature, 2000, 406: p. 775-781). Cell wall biosynthesis requires the enzyme MurI, a glutamate racemase, and therefore this enzyme is essential for bacterial viability (Doublet, P., *et al., The murI gene of Escherichia coli is an essential gene that encodes a glutamate racemase activity.* Journal of Bacteriology, 1993, 175(10): p. 2970-9).

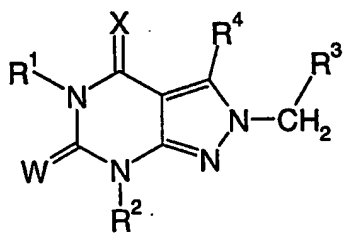
The present invention describes compounds, which specifically inhibit *H. pylori* MurI, compositions of such compounds and methods of use. The compounds disclosed herein represent a valuable contribution to the development of selective therapies directed to diseases resulting from *H. pylori* infection.

## Summary of the invention

In accordance with the present invention, the applicants have hereby discovered novel compounds that inhibit the MurI enzyme and thereby inhibit cell wall biosynthesis in *H. pylori* bacterium. The present invention includes pharmaceutically acceptable salts or prodrugs of such compounds. Also in accordance with the present invention applicants provide pharmaceutical compositions and a method to use invention compounds in the treatment of infections.

## Detailed description of the invention

In a first embodiment, the present invention provides a novel compound having structural formula (I):




(I)

wherein,

X is S, O, or $NR^{20}$, provided that when W is O, then X is not O,

X and the double bond to which it is attached can be replaced with 2 hydrogen atoms,

W is S, O, or $NR^{20}$; provided that when X is O, then W is not O;

$R^1$ is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, hydroxy, amino, or optionally substituted heterocycle;

$R^2$ is H, optionally substituted alkyl, optionally substituted alkylcycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, or optionally substituted heterocycle;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, -

$S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, $-OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_m$Het, $-O(CH_2)_mC(=O)$Het, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_m$Het, $-S(CH_2)_mC(=O)$Het, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^b$Het, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, $-OR^c$, $-NR^aR^a$, $-S(=O)_nR^c$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, $-OC(=O)R^a$, $B(OH)_2$, vicinyl $-OCH_2CH_2O-$, vicinyl $-OC_{1-2}$haloalkylO-, vicinyl $-OCH_2O-$, vicinyl $-CH_2OCH_2O-$, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

or a pharmaceutically acceptable salt thereof.

In an additional embodiment the present invention provides a compound having a structural formulaformula (I) as recited above 1 wherein:

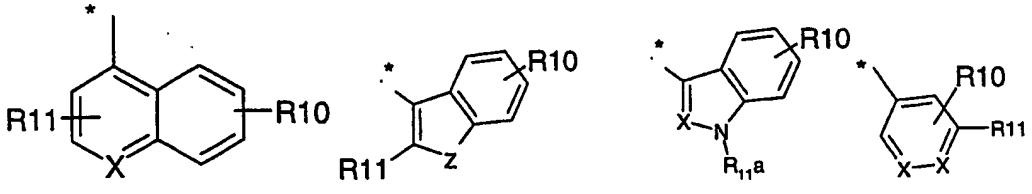
$R^1$ is H, or $C_{1-6}$alkyl, or $-(CH_2)_n$cycloalkyl or $-(CH_2)_{1-2}$Het wherein $C_{1-6}$alkyl or $-(CH_2)_n$cycloalkyl or $-(CH_2)_{1-2}$Het is optionally substituted by 1, 2 or 3 substituents selected from Het, halogen, -CN, $-OR^a$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-S(=O)_nR^c$, $-S(=O)_nNR^aR^a$ or $-NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

In an additional embodiment the present invention provides a compound having a structural formula (I) as recited above wherein:

$R^2$ is $-(CH_2)_{1-3}$cycloalkyl or $-C_{1-12}$alkyl wherein $-(CH_2)_{1-3}$cycloalkyl or $-C_{1-12}$alkyl is optionally substituted with 0, 1, 2 or 3 substituents selected from Het, $S(=O)_nR^c$, $-S(=O)_nNR^aR^a$ halogen, -CN, $-OR^a$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, or $-NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

In an additional embodiment the present invention provides a compound having a structural formula (I) as recited above wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

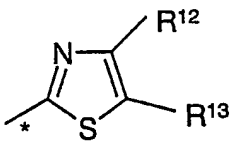


(i) (ii) (iii) (iv)

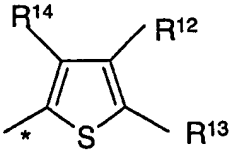
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

In an additional embodiment the present invention provides a compound having structural formulaa (I) as recited above wherein:

$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



(a)



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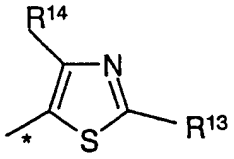

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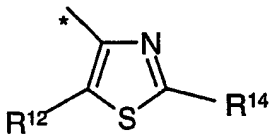

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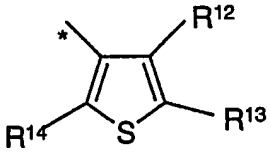

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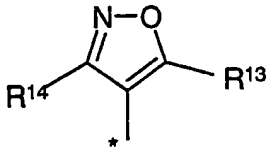

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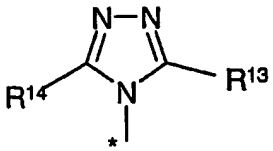

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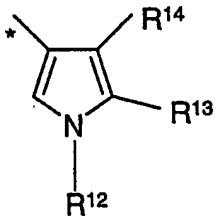

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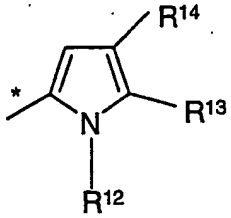
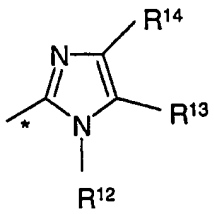
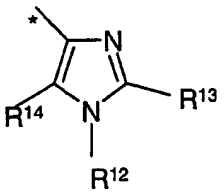


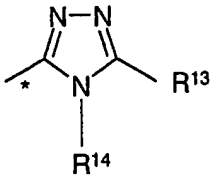
(i)



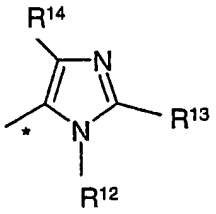

(j)




(k)




(l)

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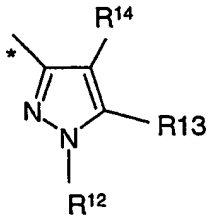
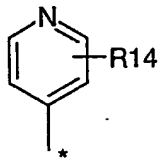
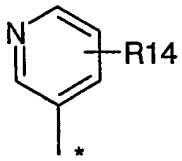



(n)




(o)

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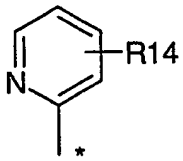


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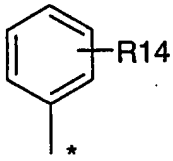


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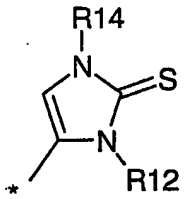


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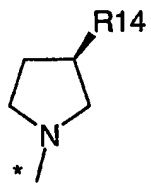


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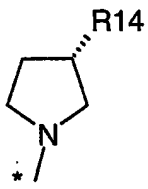


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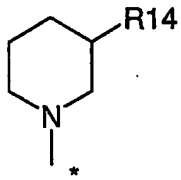


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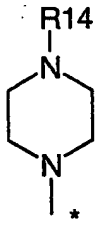


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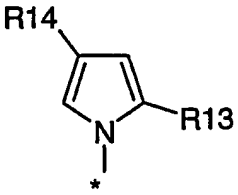


(x)

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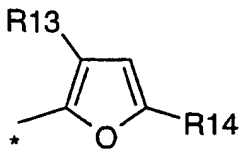


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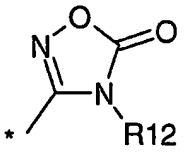
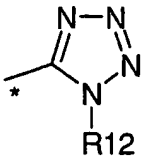
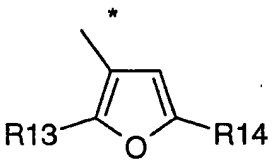



(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, $-C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound having structural formula (I) as recited above wherein:

X is S, O, or $NR^{20}$, provided that when W is O, then X is not O; or X and the double bond to which it is attached can be 2 hydrogen atoms,

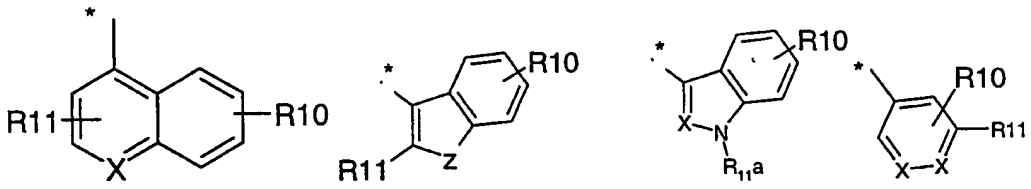
W is S, O, or $NR^{20}$; provided that when X is O, then W is not O;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

$R^2$ is $-CH_2CH_2CH_3$, $-CH_2$-cyclopropyl, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2F$, $-CH_2$-cyclobutyl, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2$-methylphenyl, $-CH_2$-phenol, $-CH_2$-(3,5-dimethylisoxazol-4-yl), $-CH_2$-S-phenyl, $-CH_2$-phenylcarboxyl, or $-CH_2SCF_3$;

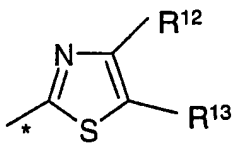
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



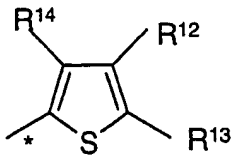

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

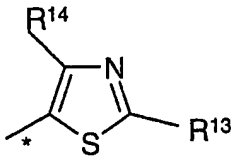
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



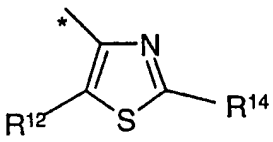
(a)



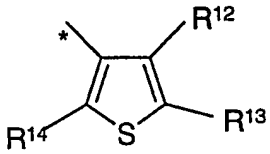
(b)



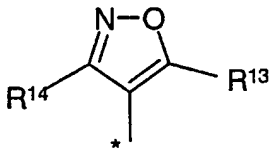
(c)



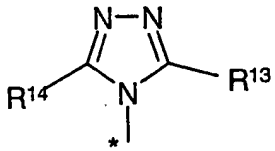
(d)



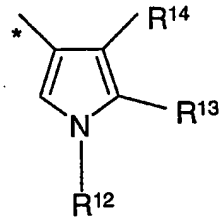
(e)



(f)



(g)



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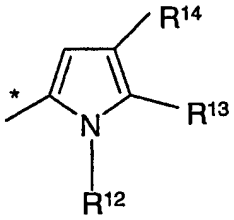
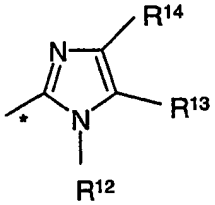


(i)



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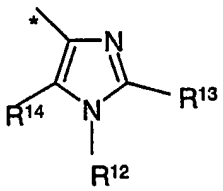
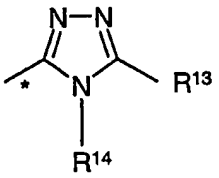
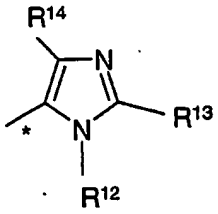


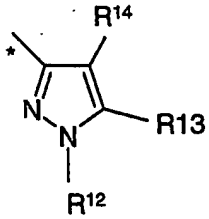
(k)



(l)



(m)



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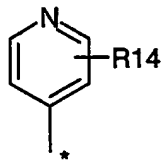

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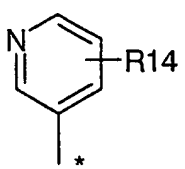


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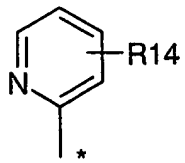


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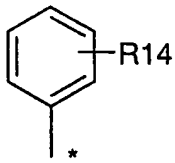


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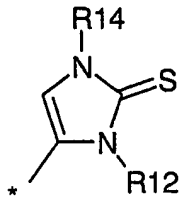


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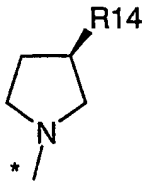


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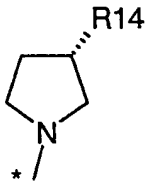


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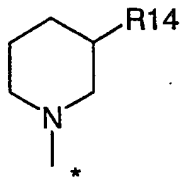


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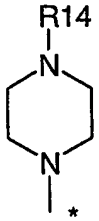


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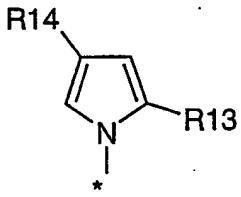
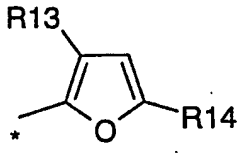
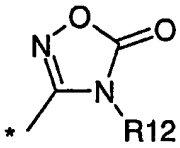



(x)




(y)

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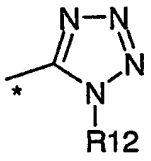


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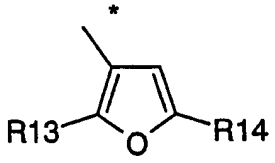



(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound selected from:

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-imino-5-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4-(methylimino)-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-imino-5-methyl-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4-oxo-6-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-6-(methylimino)-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

N-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]acetamide;

N-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]methanesulfonamide;

5-((6Z)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-{[2-(dimethylamino)ethyl]imino}-5-methyl-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)-1-methyl-1H-pyrrole-3-carbonitrile;

N~1~-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]-N~2~,N~2~-dimethylglycinamide;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

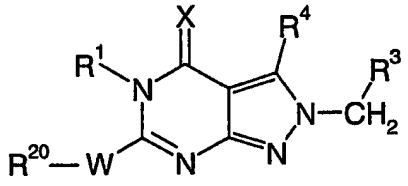
5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-thioxo-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one;

(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-(methylimino)-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one.

In a further embodiment the present invention provides a compound having the structural formula (II):



(II)

wherein,

X is S, O, or $NR^{20}$,

X and the double bond to which it is attached can be replaced with 2 hydrogen atoms,

W is S, O, or $NR^{21}$;

$R^1$ is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, hydroxy, amino, or optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl,

$C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}$alkyl)$_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, -$OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$,

$-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{21}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$; optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, -$OC(=O)R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

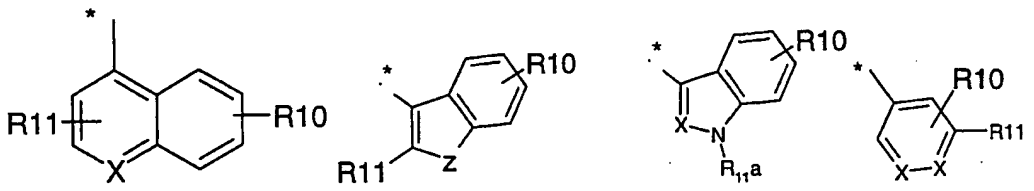
or a pharmaceutically acceptable salt thereof.

In an additional embodiment the present invention provides a compound having structural formula (II) as recited above wherein:

$R^1$ is H, or $C_{1-6}$alkyl, or –$(CH_2)_n$cycloalkyl wherein $C_{1-6}$alkyl or –$(CH_2)_n$cycloalkyl is optionally substituted by 1, 2 or 3 substituents selected from Het, halogen, -CN, -$OR^a$, -$NR^aR^a$, -$C(=O)OR^a$, -$C(=O)NR^aR^a$, -$OC(=O)C_{1-4}$alkyl or -$NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

In an additional embodiment the present invention provides a compound having structural formula (II) as recited above wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

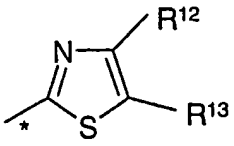



(i) (ii) (iii) (iv)

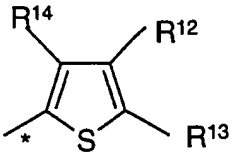
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

In an additional embodiment the present invention provides a compound having structural formula (II) as recited above wherein:

$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



(a)



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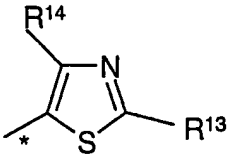
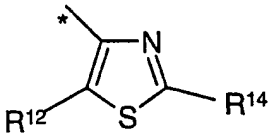
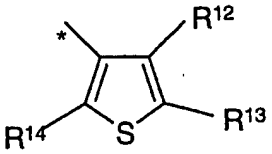


(c)



(d)



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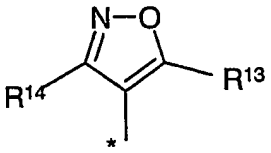
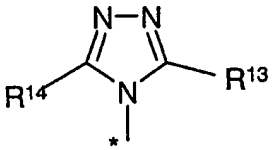
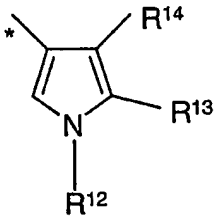


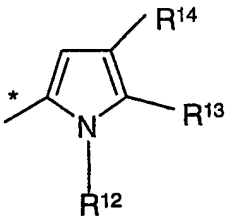
(f)



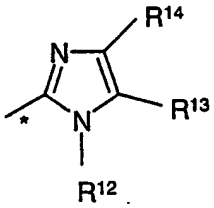
(g)



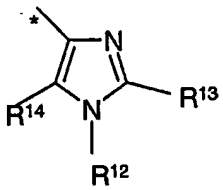
(h)



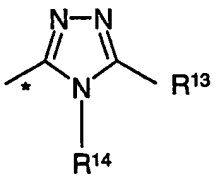
(i)



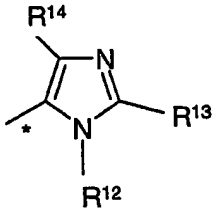
(j)



(k)



(l)



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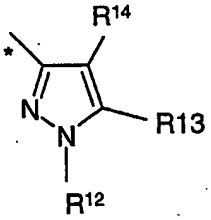

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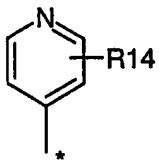

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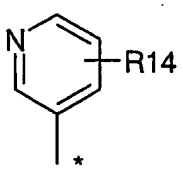


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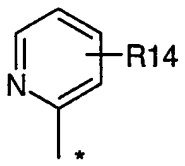


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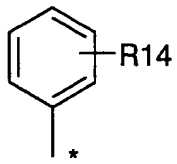


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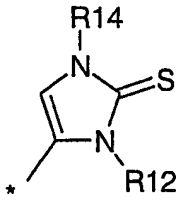


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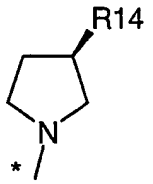


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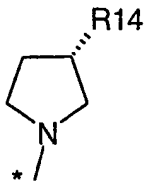


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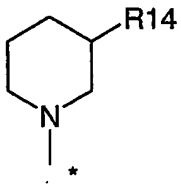


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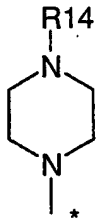
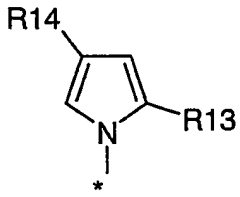



(w)

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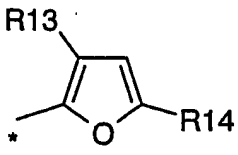


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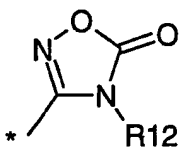


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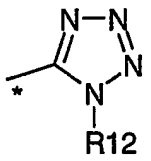
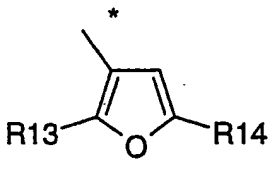



(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a)$.

In an additional embodiment the present invention provides a compound having structural formula (II) as recited above wherein:

X is S, O, or $NR^{20}$;or X and the double bond to which it is attached can be 2 hydrogen atoms,

W is S, O, or $NR^{21}$;

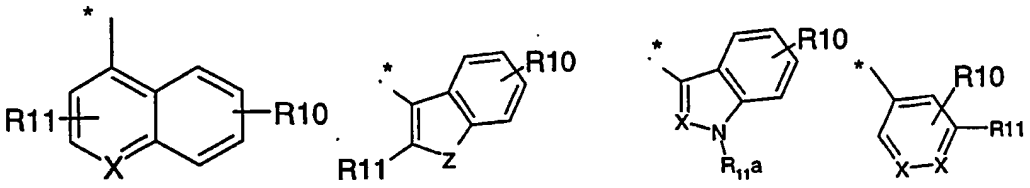
$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

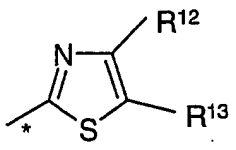
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



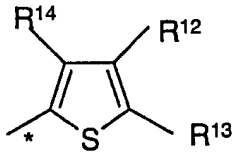

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, -

$C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

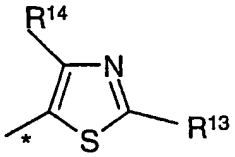
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



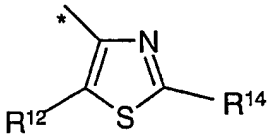
(a)



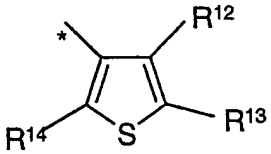
(b)



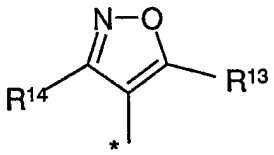
(c)



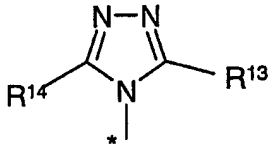
(d)



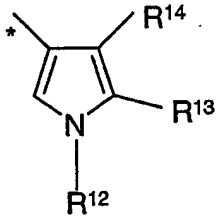
(e)



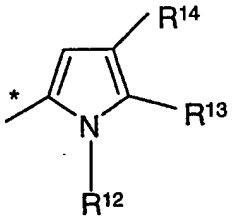
(f)



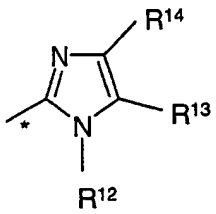
(g)



(h)



(i)

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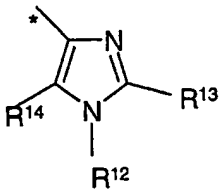
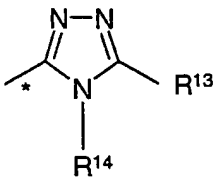
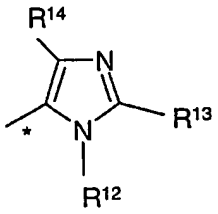


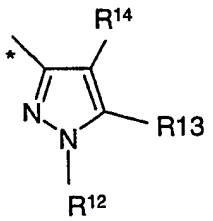

(k)



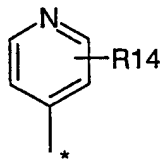

(l)




(m)




(n)

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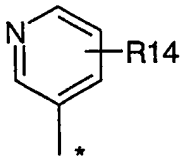


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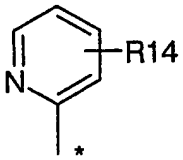


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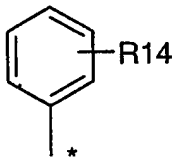


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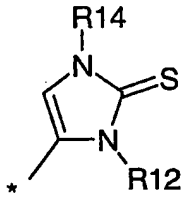


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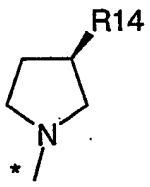
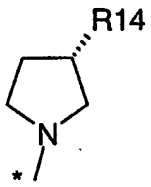



(t)

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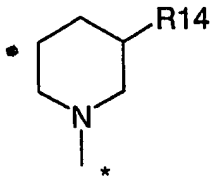


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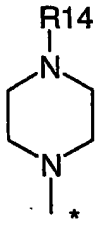


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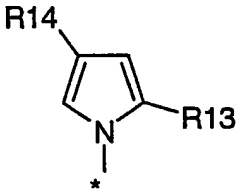
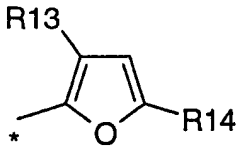
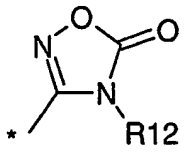



(x)

5




(y)

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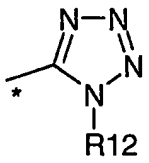


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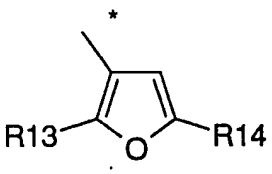



(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, $-C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound selected from:

5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-3-methylbutanamide

N,N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-3-methylbutanamide;

N'-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-N,N-dimethylimidoformamide;

5-{2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)(methyl)amino]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]propane-1-sulfonamide;

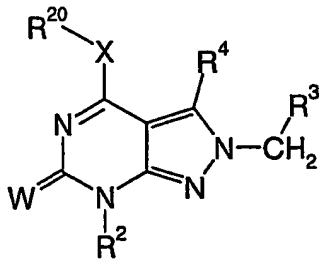
ethyl 2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-ylcarbamate;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-N'-ethylurea;

5-[(4Z)-2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-5-methyl-4-(methylimino)-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(4Z,6Z)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4,6-bis(methylimino)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile.

In a further embodiment the present invention provides a compound having structural formula (III) as recited above wherein:



(III)

wherein,

X is S, O, $NR^{21}$; or $XR^{20}$ is hydrogen;

W is S, O, or $NR^{20}$;

$R^2$ is H, optionally substituted alkyl, optionally substituted alkylcycloalkyl, optionally substituted alkylcycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted

cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, or optionally substituted heterocycle;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, -$OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, -

$C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{21}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

or

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, $-OR^c$, $-NR^aR^a$, $-S(=O)_nR^c$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, $-OC(=O)R^a$, $B(OH)_2$, vicinyl $-OCH_2CH_2O-$, vicinyl $-OC_{1-2}$haloalkylO-, vicinyl $-OCH_2O-$, vicinyl $-CH_2OCH_2O-$, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, NH($C_{1-4}$ alkyl), N($C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

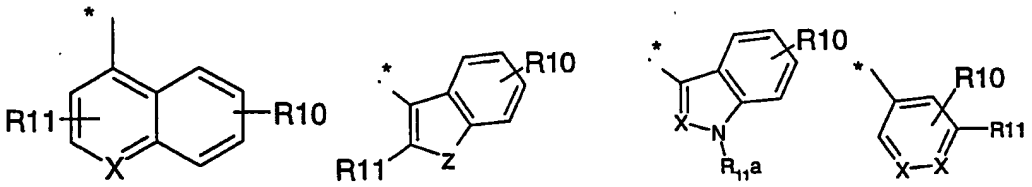
or a pharmaceutically acceptable salt thereof.

In an additional embodiment the present invention provides a compound having structural formula (III) as recited above wherein:

$R^2$ is –($CH_2$)$_{1-3}$cycloalkyl or -$C_{1-12}$alkyl wherein –($CH_2$)$_{1-3}$cycloalkyl or -$C_{1-12}$alkyl is optionally substituted with 0, 1, 2 or 3 substituents selected from Het, S(=O)$_n$$R^c$, halogen, -CN, -O$R^a$, -N$R^a$$R^a$, -C(=O)O$R^a$, -C(=O)$R^a$, -C(=O)N$R^a$$R^a$, -OC(=O)$C_{1-4}$alkyl or -N$R^a$C(=O)$C_{1-4}$alkyl and n is 0, 1 or 2.

In an additional embodiment the present invention provides a compound having structural formula (III) as recited above wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



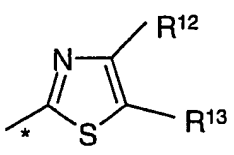

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are

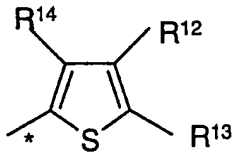
independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

In an additional embodiment the present invention provides a compound having structural formula (III) as recited above wherein:

$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



(a)



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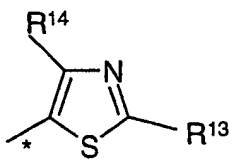

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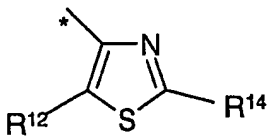

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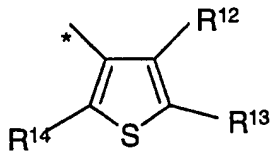

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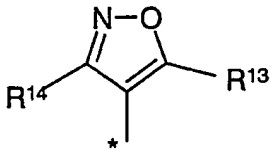

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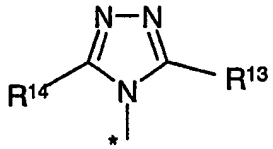
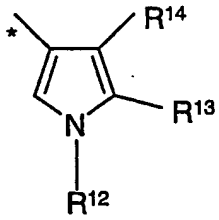


(g)



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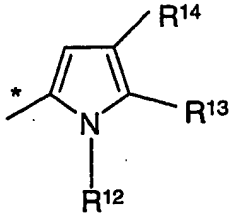

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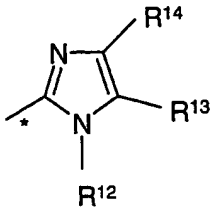

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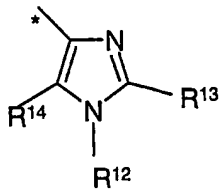
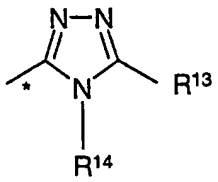
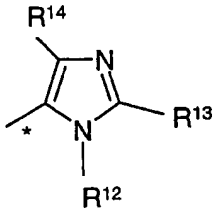


(k)



(l)



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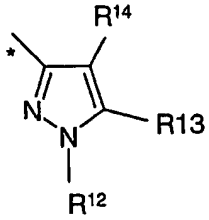
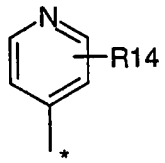


(n)



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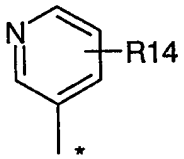

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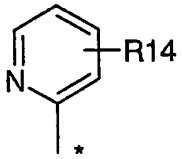

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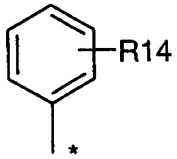
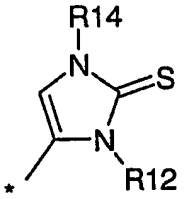
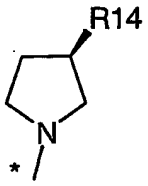


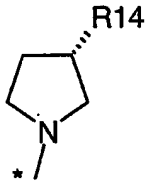
(r)



(s)



(t)



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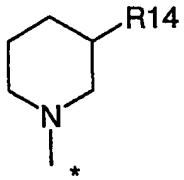
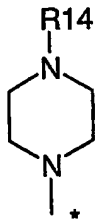
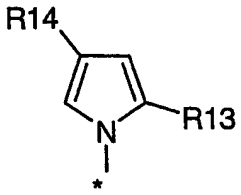


(v)



(w)



(x)

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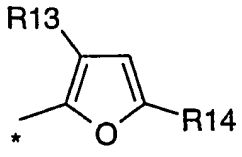
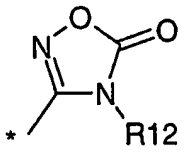
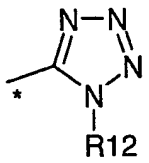


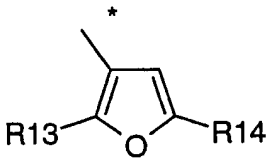

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, $-C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound having structural formula (III) as recited above wherein:

X is S, O, or $NR^{21}$;or $XR^{20}$ is hydrogen,

W is S, O, or $NR^{20}$;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

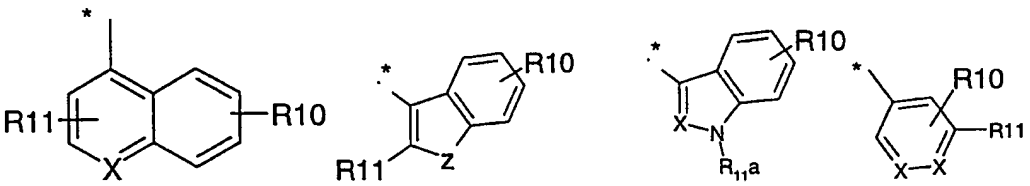
$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^c$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

$R^2$ is $-CH_2CH_2CH_3$, $-CH_2$-cyclopropyl, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2F$, $-CH_2$-cyclobutyl, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2$-methylphenyl, $-CH_2$-phenol, $-CH_2$-(3,5-dimethylisoxazol-4-yl), $-CH_2$-S-phenyl, $-CH_2$-phenylcarboxyl, or $-CH_2SCF_3$;

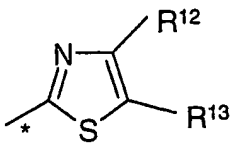
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



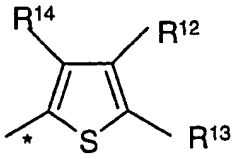

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

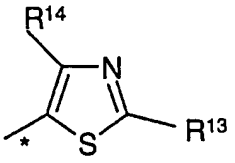
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



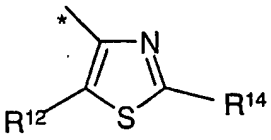
(a)



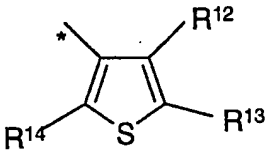
(b)



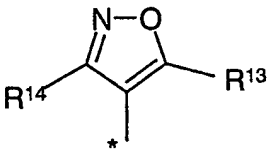
(c)



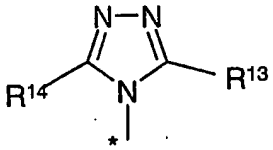
(d)



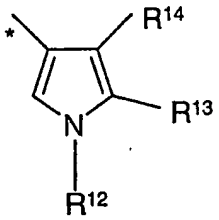
(e)



(f)



(g)



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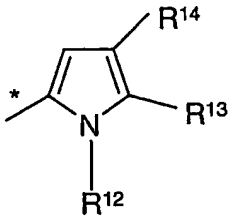
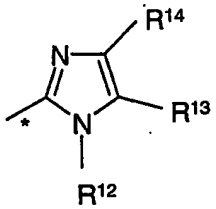
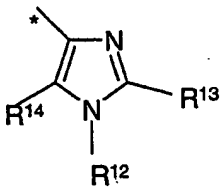


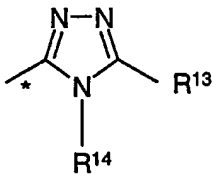
(i)



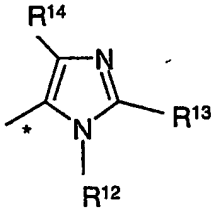
(j)



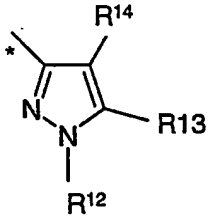
(k)



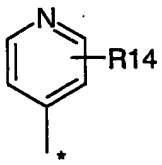
(l)



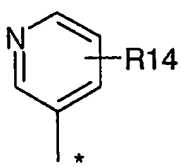
(m)



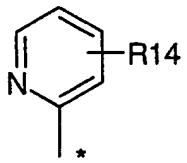
(n)



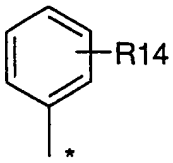
(o)



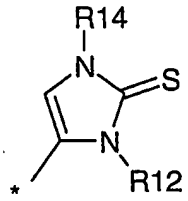

(p)



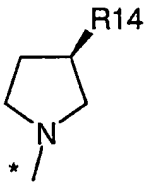

(q)



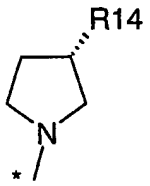

(r)




(s)




(t)

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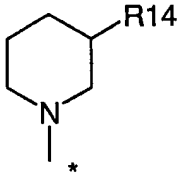


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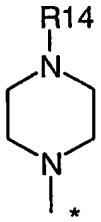
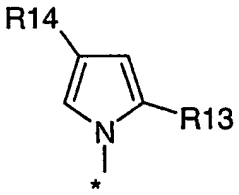
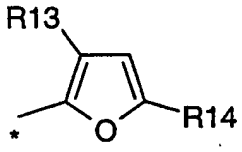


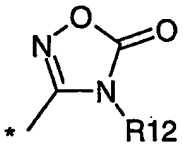

(w)




(x)




(y)

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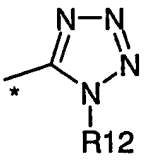
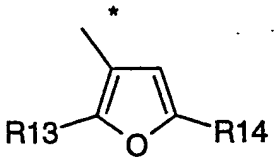



(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a-SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound selected from:

4-amino-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

7-isobutyl-4-(methylamino)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

4-(dimethylamino)-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

7-isobutyl-4-(4-methylpiperazin-1-yl)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-3-(1-methyl-1H-pyrrol-2-yl)-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

5-{4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-4-(methylamino)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(dimethylamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-4-(propylamino)-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-4-[(2-hydroxyethyl)amino]-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(hydroxyamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(cyclopropylamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-4-hydrazino-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(2,2-dimethylhydrazino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-4-yl]acetamide;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-(methylthio)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(2-hydroxybutyl)amino]-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-(2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-{[(2R)-2-hydroxypropyl]amino}-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)-1-methyl-1H-pyrrole-3-carbonitrile;

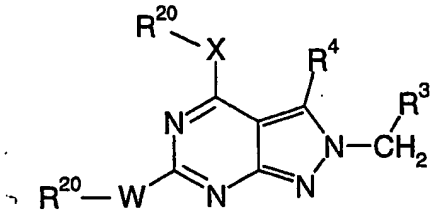
5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-methoxy-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-(1*H*-pyrrol-1-yl)-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(6*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-(methylamino)-6-(methylimino)-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

In a further embodiment the present invention provides a compound having structural formula (IV),



(IV)

wherein,

X is S, O, $NR^{21}$ ; or $XR^{20}$ is hydrogen;

W is S, O, or $NR^{21}$;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, -$OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, -

$C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein such substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{21}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$; optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle wherein such substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, -$OC(=O)R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

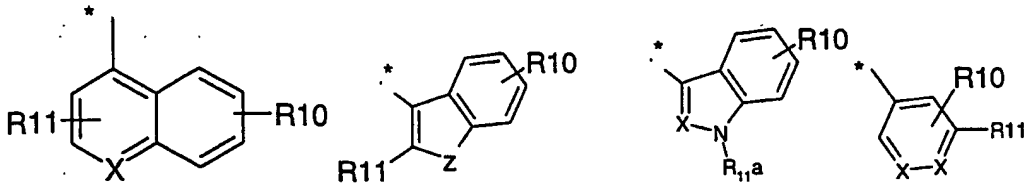
n is 0, 1 or 2;

When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

or a pharmaceutically acceptable salt thereof.

In an additional embodiment the present invention provides a compound having structural formula (IV) as recited above wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

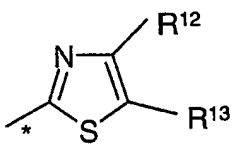



(i) (ii) (iii) (iv)

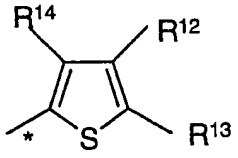
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

In an additional embodiment the present invention provides a compound having structural formula (IV) as recited above wherein:

$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



(a)



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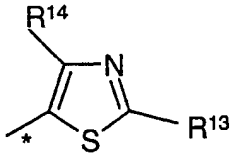
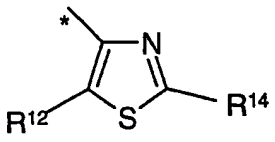
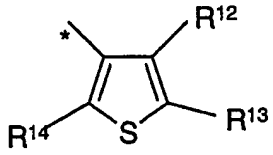


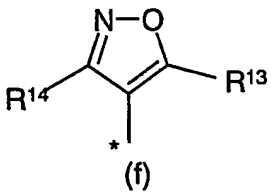
(c)



(d)



(e)



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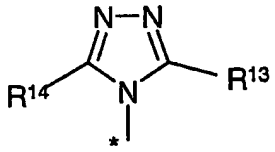

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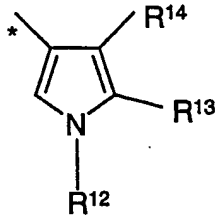

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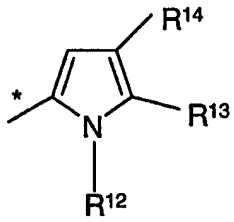
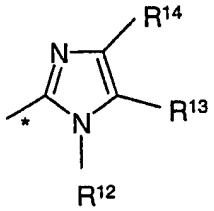
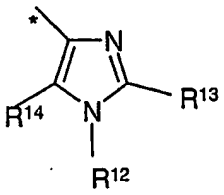


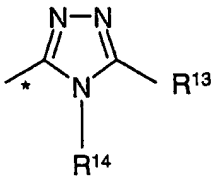
(i)



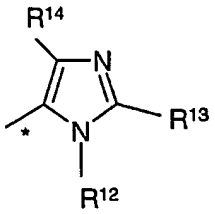

(j)



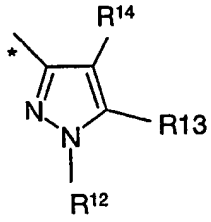

(k)




(l)




(m)

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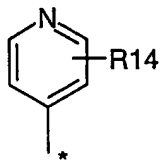
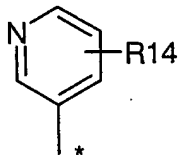
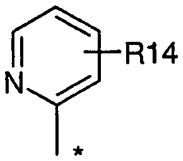


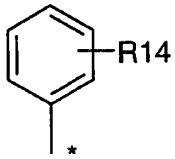

(o)



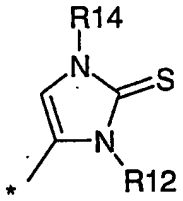

(p)



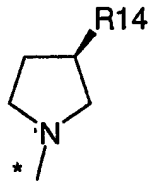

(q)



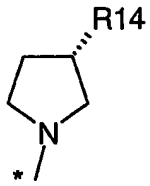

(r)




(s)




(t)

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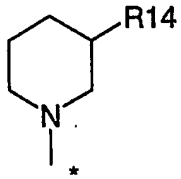
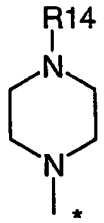
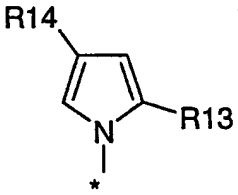


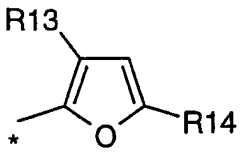

(v)



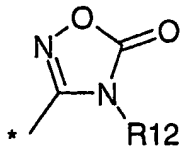

(w)



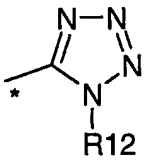

(x)



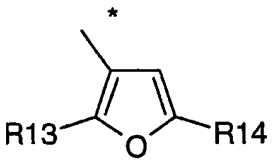

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -$C(=O)NR^aNR^aR^a$, -$C(=O)NR^a(R^bNR^aR^a)$, -$C(=O)NR^a(R^bOR^a)$, -$C(=O)NR^a(R^bS(=O)_2R^a)$, -$C(=O)NR^aR^b$Het, -$C(=O)NR^aOR^a$, -$C(=O)R^bNR^aR^a$, -$C(=NOR^a)R^a$, -$C(=NCN)R^a$, -$C(=O)OR^a$, -$C(=O)OR^bNR^aR^a$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)R^a$-$SR^a$, =S, -$NR^aC(=O)R^a$, -$NR^aC(=O)OR^a$, -$NR^aS(=O)_2R^b$, -$C(=NOR^a)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^aR^a$, -$S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or -$S(=O)_2NR^a(R^bC(=O)OR^a$.

In an additional embodiment the present invention provides a compound having structural formula (IV) as recited above wherein:

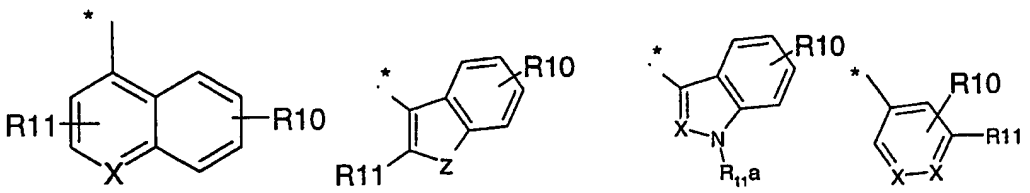
X is S, O, or $NR^{21}$; or X-$R^{20}$ is hydrogen

W is S, O, or $NR^{21}$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, -$CH_2$-2-pyridyl, -$CH_2$-3-pyridyl, -$CH_2$-4-pyridyl, -$(CH_2)_2$-1-imidazolyl, -$(CH_2)_2$-1-pyrazolyl, -$(CH_2)_2$-1-piperidyl, -$(CH_2)_m$-(1-methylpiperidin-4-yl), -$CH_2$-(1-methylpiperidin-3-yl), -$(CH_2)_2$-(morpholin-4-yl),

$R^2$ is -$CH_2CH_2CH_3$, -$CH_2$-cyclopropyl, -$CH_2CH(CH_3)_2$, -$CH_2CH_2CH_2F$, -$CH_2$-cyclobutyl, -$CH_2C(CH_3)_3$, -$CH_2CH_2CH(CH_3)_2$, -$CH_2CF_3$, -$CH_2$-methylphenyl, -$CH_2$-phenol, -$CH_2$-(3,5-dimethylisoxazol-4-yl), -$CH_2$-S-phenyl, -$CH_2$-phenylcarboxyl, or -$CH_2SCF_3$;

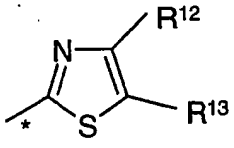
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



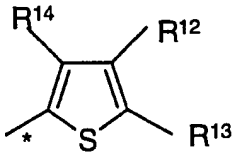

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

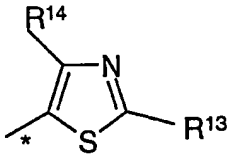
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



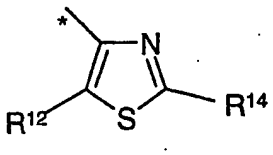

(a)



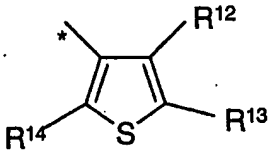

(b)



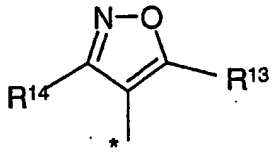

(c)



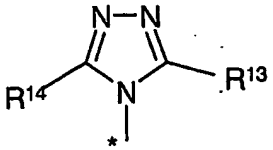

(d)



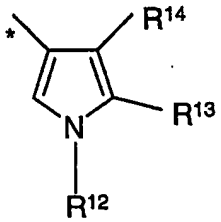

(e)



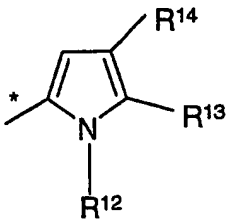

(f)



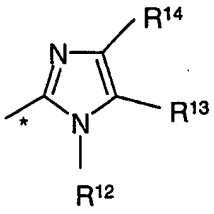

(g)



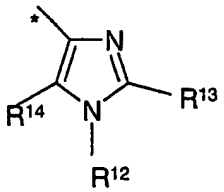

(h)



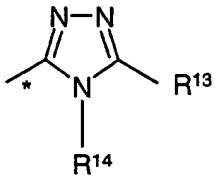

(i)



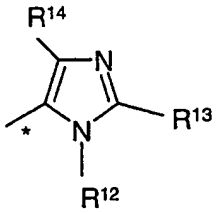

(j)



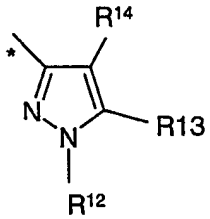

(k)



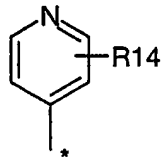

(l)



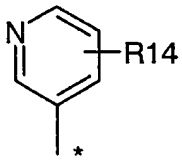

(m)



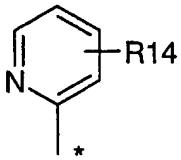

(n)



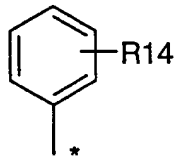

(o)



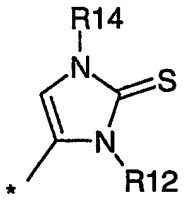

(p)



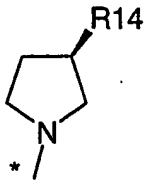

(q)



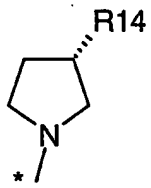

(r)



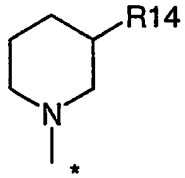

(s)



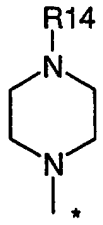

(t)




(u)




(v)

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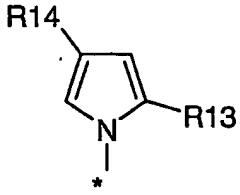
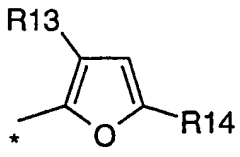
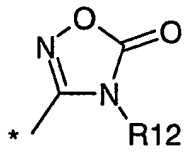



(x)

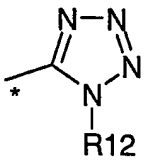
5



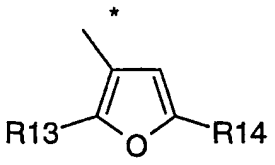

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -$C(=O)NR^aNR^aR^a$, -$C(=O)NR^a(R^bNR^aR^a)$, -$C(=O)NR^a(R^bOR^a)$, -$C(=O)NR^a(R^bS(=O)_2R^a)$, -$C(=O)NR^aR^b$Het, -$C(=O)NR^aOR^a$, -$C(=O)R^bNR^aR^a$, -$C(=NOR^a)R^a$, -$C(=NCN)R^a$, -$C(=O)OR^a$, -$C(=O)OR^bNR^aR^a$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)R^a$-$SR^a$, =S, -$NR^aC(=O)R^a$, -$NR^aC(=O)OR^a$, -$NR^aS(=O)_2R^b$, -$C(=NOR^a)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^aR^a$, -$S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or -$S(=O)_2NR^a(R^bC(=O)OR^a$.

$R^{20}$ is H, -CN, $R^a$, -$OR^a$, -$NR^aR^a$, -Het, -$S(=O)_nR^c$, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, or -$OC(=O)R^a$;

$R^{20}$ is H, -CN, $R^a$, -$OR^a$, -$NR^aR^a$, -Het, -$S(=O)_nR^c$, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, or -$OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -$C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S.

In an additional embodiment the present invention provides a compound selected from:

5-[2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-4-(methylamino)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

*N*-{3-(4-acetyl-1-methyl-1*H*-pyrrol-2-yl)-2-[(6-chloroquinolin-4-yl)methyl]-4-methoxy-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl}-2-cyclopropylacetamide.

In a further embodiment the present invention provides a compound according to any one of claims 1 to 24, for use as a medicament.

In a further embodiment the present invention provides the use of a compound as defined in any one of claims 1 to 24, in the manufacture of a medicament for the treatment or prophylaxis of disorders associated with *H. pylori* infection.

In a further embodiment the present invention provides a method for the treatment of infections associated with *H. pylori* comprising administering to a host in need of such treatment a therapeutically effective amount of a compound as defined in any one of formulas (I), (II), (III), (IV).

In a further embodiment the present invention provides a method for the prophylaxis treatment of infections associated with *H. pylori* comprising administering to a host in need of such treatment a therapeutically effective amount of a compound as defined in any one of formulas (I), (II), (III), (IV).

In a further embodiment the present invention provides a method for the treatment or prophylaxis of *H. pylori* infection comprising administering a therapeutically effective amount of a compound as defined in any one of formulas (I), (II), (III), (IV).

In a further embodiment the present invention provides a pharmaceutical composition comprising a compound as defined in any one of formulas (I), (II), (III), (IV) together with at least one pharmaceutically acceptable carrier, diluent or excipent.

**Definitions**

The definitions set forth in this section are intended to clarify terms used throughout this application. The term "herein" means the entire application.

As used in this application, the term "optionally substituted," as used herein, means that substitution is optional and therefore it is possible for the designated atom to be unsubstituted. In the event a substitution is desired then such substitution means that any number of hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. For example when a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

When any variable (e.g., $R^1$, $R^4$, $R^a$, $R^e$ etc.) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-3 $R^1$, then said group may optionally be substituted with 0,1, 2 or 3 $R^1$ groups and $R^e$ at each occurrence is selected independently from the definition of $R^e$. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. When required, separation of the racemic material can be achieved by methods known in the art. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without

indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein "acyl" refers to groups of the of the general formula –C(=O)-R, wherein R is hydrogen, hydrocarbyl radical, amino or alkoxy. Examples of acyl groups include, but are not limited to acetyl, propionyl, benzoyl, phenyl acetyl, carboethoxy, and dimethylcarbamoyl.

As used herein the term "amine" or "amino" refers to groups of the general formula –NRR', wherein R and R' are independently selected from hydrogen or a hydrocarbyl radical.

As used herein "aromatic" refers to hydrocarbyl groups having one or more polyunsaturated carbon rings having aromatic character, (e.g., 4n + 2 delocalized electrons) and comprising up to about 14 carbon atoms.

As used herein, "alkyl" or "alkylene" used alone or as a suffix or prefix, is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having from 1 to 12 carbon atoms or if a specified number of carbon atoms is provided then that specific number would be intended. For example "$C_{1-6}$ alkyl" denotes alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, pentyl, and hexyl. As used herein, "$C_{1-3}$ alkyl", whether a terminal substituent or an alkylene group linking two substituents, is understood to specifically include both branched and straight-chain methyl, ethyl, and propyl.

As used herein, "alkenyl" or "alkenylene" is intended to include from 2 to 12 hydrocarbon atoms of either a straight or branched configuration with one or more carbon-carbon double bonds that may occur at any stable point along the chain. Examples of "$C_{3-6}$alkenyl" include, but are not limited to, 1-propenyl, 2-propenyl, 1-butenyl, 2-butenyl, 3-butenyl, 3-methyl-2-butenyl, 2-pentenyl, 3-pentenyl, hexenyl.

As used herein, "alkynyl" or "alkynylene" is intended to include from 2 to 12 hydrocarbon chains of either a straight or branched configuration with one or more carbon-carbon triple

bonds that may occur at any stable point along the chain. Examples of alkynyl include but are not limited to ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl.

As used herein, "alkoxy" or "alkyloxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, t-butoxy, n-pentoxy, isopentoxy, cyclopropylmethoxy, allyloxy and propargyloxy. Similarly, "alkylthio" or "thioalkoxy" represent an alkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

As used herein, the term "aryl" is intended to mean aromatic groups including both monocyclic aromatic groups comprising 6 carbon atoms and polycyclic aromatic groups comprising up to about 14 carbon atoms.

As used herein the term "cycloalkyl" is intended to include saturated ring groups, having the specified number of carbon atoms. For example, "$C_{3-6}$ cycloalkyl" denotes such groups as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

As used herein the term "alkylcycloalkyl" is intended to mean an alkyl attached to the formula atom modified with a cycloalkyl. Examples of alkylcycloalkyl include, but are not limited to cyclopropylmethyl, cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl, cyclopropylethyl, cyclopentylethyl, cyclohexylethyl, cycloheptylethyl, cyclopropylpropyl, cyclopentylpropyl, cyclohexylpropyl, cycloheptylpropyl.

As used herein "cycloalkenyl" refers to ring-containing hydrocarbyl groups having at least one carbon-carbon double bond in the ring, and having from 3 to 12 carbons atoms.

As used herein "cycloalkynyl" refers to ring-containing hydrocarbyl groups having at least one carbon-carbon triple bond in the ring, and having from 7 to 12 carbons atoms.

As used herein, "electronically neutral" refers to a stable compound having a no charge.

As used herein, "halo" or "halogen" refers to fluoro, chloro, bromo, and iodo. "Counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, sulfate, tosylate, benezensulfonate, and the like.

As used herein, "haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example --$C_vF_w$ where v=1 to 3 and w=1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, pentachloroethyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, heptafluoropropyl, and heptachloropropyl. "Haloalkoxy" is intended to mean a haloalkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge; for example trifluoromethoxy, pentafluoroethoxy, 2,2,2-trifluoroethoxy, and the like. "Haloalkylthio" is intended to mean a haloalkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

As used herein, the term "Het" is intended to mean a 5 or 6 member ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S, and substituted by 0, 1, 2 or 3 substituents selected from halogen, $C_{1-4}$alkyl, $-S(=O)_nR^c$, $-C(=O)R^a$, or $-S(=O)_2NR^aR^a$, vicinal $-OCH_2CH_2O-$, vicinal $-OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, ,or vicinal $-CH_2OCH_2O-$, =O, halogen, cyano, $-R^bOR^a$, $-R^bSR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, -OH, $-NHR^a$, $-NR^a{}_2$, $-NHC(=O)R^a$, $N=NR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^b$Het, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

As used herein, the term "heterocycle" or "heterocyclic" or hetercyclyl refers to a ring-containing monovalent and divalent structures having one or more heteroatoms, independently selected from N, O and S, as part of the ring structure and comprising from 3 to 20 atoms in the rings. Heterocyclic groups may be saturated or unsaturated, containing one or more double bonds, and heterocyclic groups may contain more that one ring. The heterocyclic rings described herein may be substituted on carbon or on a heteroatom atom if the resulting compound is stable. If specifically noted, nitrogen in the heterocycle may

optionally be quaternized. It is understood that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another.

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H, 6H-1, 5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1, 2,5-thiadiazinyl, acridinyl, azetidine, aziridine, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benzotriazolyl, benzotetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4aH-carbazolyl, b-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dioxolane, furyl, 2,3-dihydrofuran, 2,5-dihydrofuran, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, homopiperidinyl, imidazolidine, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxirane, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, purinyl, pyranyl, pyrrolidine, pyrroline, pyrrolidine, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, N-oxide-pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, thiophane, thiotetrahydroquinolinyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, thiirane, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, xanthenyl.

In addition to the polycyclic heterocycles described above, heterocyclic or heterocycle compounds include polycyclic heterocyclic moieties wherein the ring fusion between two or more rings comprises more than one bond common to both rings and more than two atoms common to both rings. Examples of such bridged heterocycles include quinuclidine, diazabicyclo[2.2.1]heptane and 7-oxabicyclo[2.2.1]heptane.

As used herein, "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, maleic, tartaric, citric, ascorbic, palmitic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are intended to include any covalently bonded carriers that release the active parent drug according to formula (I) in vivo when such prodrug is administered to a mammalian subject. Prodrugs of a compound of formula (I) are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved,

either in routine manipulation or in vivo, to the parent compound. Prodrugs include compounds of formula (I) wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula (I) is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of formula (I), and the like.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

**Formulations**

Compounds of the present invention may be administered orally, parenteral, buccal, vaginal, rectal, inhalation, insufflation, sublingually, intramuscularly, subcutaneously, topically, intranasally, intraperitoneally, intrathoracially, intravenously, epidurally, intrathecally, intracerebroventricularly and by injection into the joints.

The dosage will depend on the route of administration, the severity of the disease, age and weight of the patient and other factors normally considered by the attending physician, when determining the individual regimen and dosage level as the most appropriate for a particular patient.

An effective amount of a compound of the present invention for use in therapy of infection is an amount sufficient to symptomatically relieve in a warm-blooded animal, particularly a human the symptoms of infection, to slow the progression of infection, or to reduce in patients with symptoms of infection the risk of getting worse.

For preparing pharmaceutical compositions from the compounds of this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets, and suppositories.

A solid carrier can be one or more substances, which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, or tablet disintegrating agents; it can also be an encapsulating material.

In powders, the carrier is a finely divided solid, which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

For preparing suppository compositions, a low-melting wax such as a mixture of fatty acid glycerides and cocoa butter is first melted and the active ingredient is dispersed therein by, for example, stirring. The molten homogeneous mixture is then poured into convenient sized molds and allowed to cool and solidify.

Suitable carriers include magnesium carbonate, magnesium stearate, talc, lactose, sugar, pectin, dextrin, starch, tragacanth, methyl cellulose, sodium carboxymethyl cellulose, a low-melting wax, cocoa butter, and the like.

Some of the compounds of the present invention are capable of forming salts with various inorganic and organic acids and bases and such salts are also within the scope of this invention. Examples of such acid addition salts include acetate, adipate, ascorbate, benzoate, benzenesulfonate, bicarbonate, bisulfate, butyrate, camphorate, camphorsulfonate, choline, citrate, cyclohexyl sulfamate, diethylenediamine, ethanesulfonate, fumarate, glutamate, glycolate, hemisulfate, 2-hydroxyethylsulfonate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, hydroxymaleate, lactate, malate, maleate, methanesulfonate, meglumine, 2-naphthalenesulfonate, nitrate, oxalate, pamoate, persulfate, phenylacetate, phosphate, diphosphate, picrate, pivalate, propionate, quinate, salicylate, stearate, succinate, sulfamate, sulfanilate, sulfate, tartrate, tosylate (p-toluenesulfonate), trifluoroacetate, and undecanoate. Base salts include ammonium salts, alkali metal salts such as sodium, lithium and potassium salts, alkaline earth metal salts such as aluminum, calcium and magnesium salts, salts with organic bases such as dicyclohexylamine salts, N-methyl-D-glucamine, and salts with amino acids such as arginine, lysine, ornithine, and so forth. Also, basic nitrogen-containing groups may be quaternized with such agents as: lower alkyl halides, such as methyl, ethyl, propyl, and butyl halides; dialkyl sulfates like dimethyl, diethyl, dibutyl; diamyl sulfates; long chain halides such as decyl, lauryl, myristyl and stearyl halides; aralkyl halides like benzyl bromide and others. Non-toxic physiologically-acceptable salts are preferred, although other salts are also useful, such as in isolating or purifying the product.

The salts may be formed by conventional means, such as by reacting the free base form of the product with one or more equivalents of the appropriate acid in a solvent or medium in which the salt is insoluble, or in a solvent such as water, which is removed *in*

*vacuo* or by freeze drying or by exchanging the anions of an existing salt for another anion on a suitable ion-exchange resin.

In order to use a compound of the formula (I) or a pharmaceutically acceptable salt thereof for the therapeutic treatment (including prophylactic treatment) of mammals including humans, it is normally formulated in accordance with standard pharmaceutical practice as a pharmaceutical composition.

In addition to the compounds of the present invention, the pharmaceutical composition of this invention may also contain, or be co-administered (simultaneously or sequentially) with, one or more pharmacological agents of value in treating one or more disease conditions referred to herein.

The term composition is intended to include the formulation of the active component or a pharmaceutically acceptable salt with a pharmaceutically acceptable carrier. For example this invention may be formulated by means known in the art into the form of, for example, tablets, capsules, aqueous or oily solutions, suspensions, emulsions, creams, ointments, gels, nasal sprays, suppositories, finely divided powders or aerosols or nebulisers for inhalation, and for parenteral use (including intravenous, intramuscular or infusion) sterile aqueous or oily solutions or suspensions or sterile emulsions.

Liquid form compositions include solutions, suspensions, and emulsions. Sterile water or water-propylene glycol solutions of the active compounds may be mentioned as an example of liquid preparations suitable for parenteral administration. Liquid compositions can also be formulated in solution in aqueous polyethylene glycol solution. Aqueous solutions for oral administration can be prepared by dissolving the active component in water and adding suitable colorants, flavoring agents, stabilizers, and thickening agents as desired. Aqueous suspensions for oral use can be made by dispersing the finely divided active component in water together with a viscous material such as natural synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other suspending agents known to the pharmaceutical formulation art.

The pharmaceutical compositions can be in unit dosage form. In such form, the composition is divided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of the preparations, for example, packeted tablets, capsules, and powders in vials or ampoules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

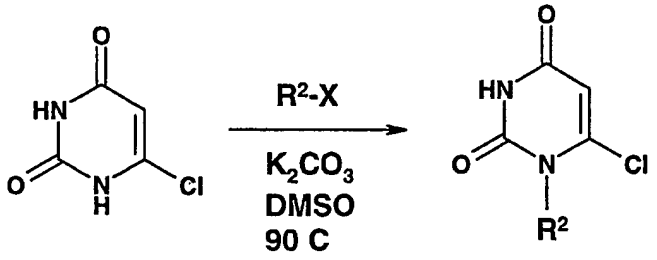
Synthesis

The compounds of the present invention can be prepared in a number of ways well known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Such methods include, but are not limited to, those described below. All references cited herein are hereby incorporated in their entirety by reference.

The novel compounds of this invention may be prepared using the reactions and techniques described herein. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being effected. Also, in the description of the synthetic methods described below, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule must be compatible with the reagents and reactions proposed. Such restrictions to the substituents, which are compatible with the reaction conditions, will be readily apparent to one skilled in the art and alternate methods must then be used.

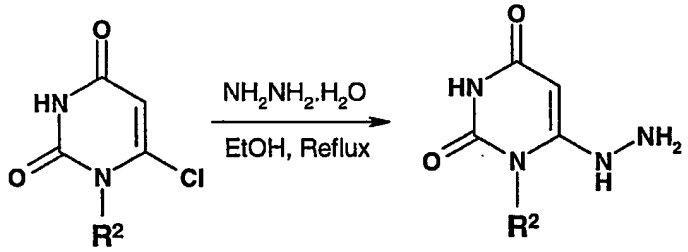
Examples of such processes are illustrated below:

In an aspect of the invention, intermediate compounds of formula **Ib** may be formed by reacting compounds of formula **Ia** with $R^2$-X in a solvent such as DMSO and a base such as $K_2CO_3$ with heat as set forth below:



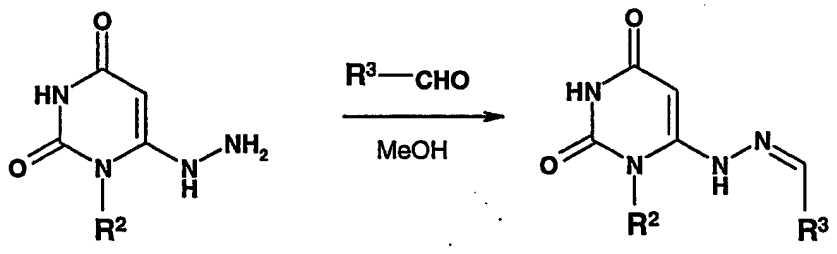

(Ia) (Ib)

An intermediate compound of formula **Ic** may be formed by reacting a compound of Formula **Ib** with $NH_2NH_2H_2O$ in ethanol and refluxed as follows:



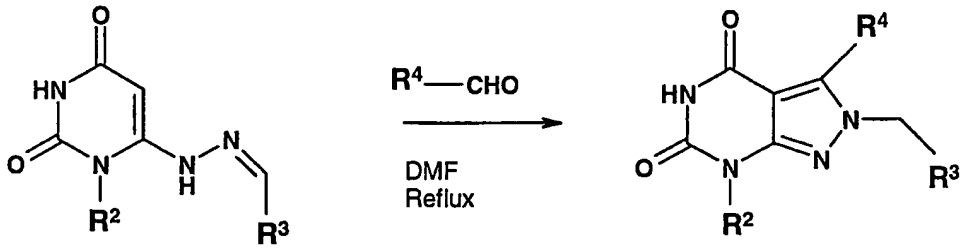

(Ib) (Ic)

Intermediate compound of Formula **Id** may be formed by reacting compounds of formula **Ic** with $R^3$-CHO in methanol as follows:



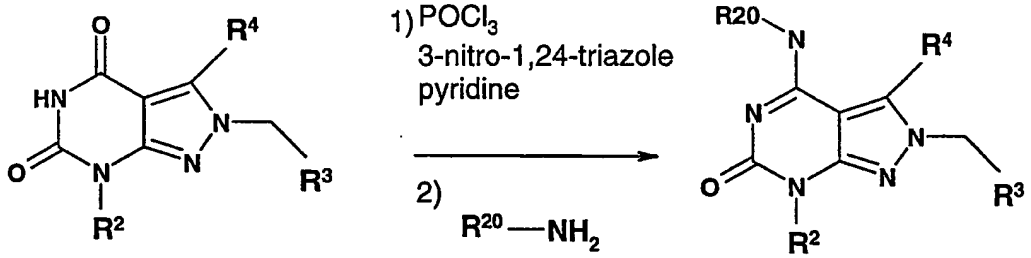

(Ic) (Id)

Intermediate compounds of formula **Ie** may by formed by reacting compounds of formula **Id** with $R^4$-CHO and reflux in DMF with piperdine as follows:



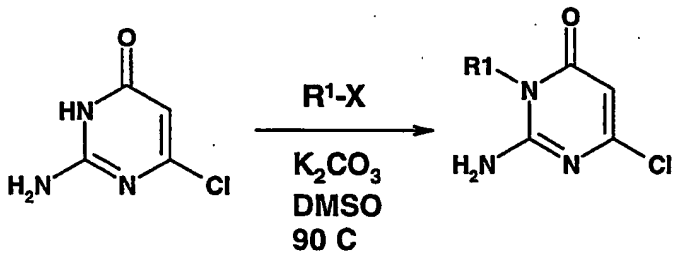

(Id) (Ie)

Compounds of formula **I** may by formed by reacting compounds of formula **Ie** with $POCl_3$, 3-nitro-1,2,4 triazole in pyridine at 70 C followed by amine ($R^{20}$-$NH_2$) as set forth below:



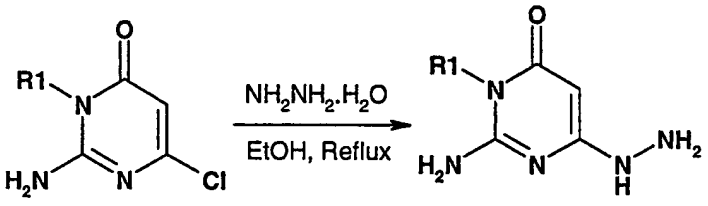

(Ie) (I)

In an aspect of the invention, intermediate compounds of formula **IIb** may be formed by reacting compounds of formula **IIa** with $R^2$-X in a solvent such as DMSO and a base such as $K_2CO_3$ with heat as set forth below:



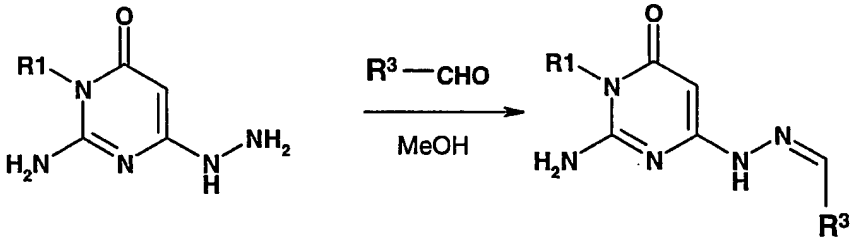

(IIa) (IIb)

An intermediate compound of formula **IIc** may be formed by reacting compounds of formula **IIb** with $NH_2NH_2H_2O$ in ethanol and refluxed as follows:



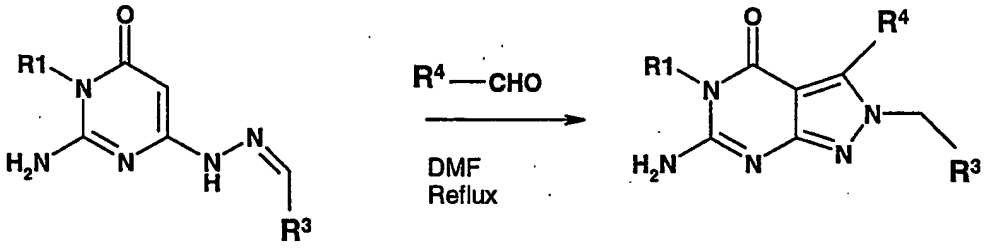

(IIb) (IIc)

Intermediate compound of formula **IId** may be formed by reacting compounds of formula **IIc** with $R^3$-CHO in methanol as follows:



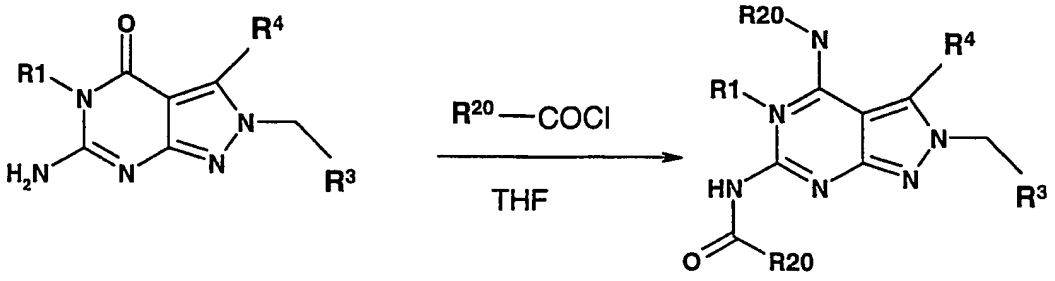

(IIc) (IId)

Intermediate compounds of formula **IIe** may by formed by reacting compounds of **IId** with $R^4$-CHO and reflux in DMF with piperdine as follows:



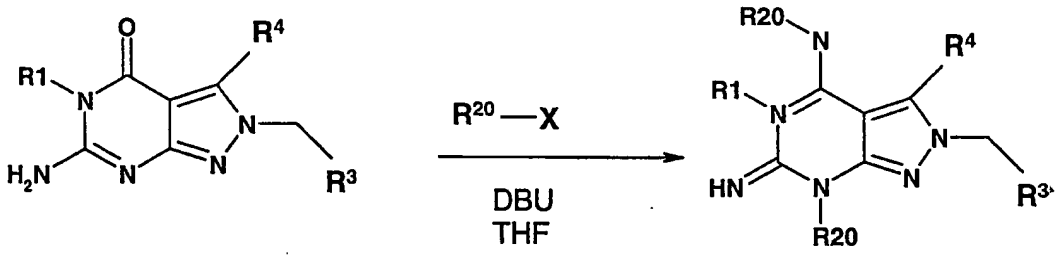

(IId) (IIe)

Compounds of formula **II** may by formed by reacting compounds of formula **IIe** with acyl chloride in ($R^{20}$-COCl) as set forth below:




(IIe) (II)

In an aspect of the invention, compounds of formula **III** may be formed by reacting compounds of formula **IIe** with $R^2$-X in a solvent such as THF and a base such as DBU with heat as set forth below:




(IIe) (III)

**Examples**

Chemical abbreviations used in the Examples are defined as follows: Boc denotes t-butoxycarbonyl, Cbz denotes benzyloxycarbonyl, DCM denotes methylene chloride, DIPEA denotes diisopropylethylamine, DMF denotes N,N-dimethylformamide, DMSO denotes dimethyl sulfoxide, $Et_2O$ denotes diethyl ether, EtOAc denotes ethyl acetate, TFA denotes trifluoroacetic acid, THF denotes tetrahydrofuran. Solvent mixture compositions are given as volume percentages or volume ratios. In cases where the NMR spectrum is complex, only diagnostic signals are reported.

Other terms used in the Examples are defined as follows: atm. denotes atmospheric pressure, equiv. denotes equivalent(s), h denotes hour(s), $T_b$denotes bath temperature, HPLC denotes

high performance liquid chromatography, min denotes minutes, NMR denotes nuclear magnetic resonance, psi denotes pounds per square inch.

(i) temperatures are given in degrees Celsius (°C); unless otherwise stated, operations were carried out at room or ambient temperature, that is, at a temperature in the range of 18-25 °C;

(ii) organic solutions were dried over anhydrous magnesium sulfate or sodium sulfate; evaporation of solvent was carried out using a rotary evaporator under reduced pressure (600-4000 Pascals; 4.5-30 mm Hg) with a bath temperature of up to 60 °C;

(iii) chromatography means flash chromatography on silica gel or by FlashMaster™ II by Jones Chromatography using Isolute columns; thin layer chromatography (TLC) was carried out on silica gel plates;

(iv) in general, the course of reactions was followed by TLC or analytical HPLC and reaction times are given for illustration only;

(v) melting points are uncorrected and (dec) indicates decomposition;

(vi) final products had satisfactory proton nuclear magnetic resonance (NMR) spectra;

(vii) when given, NMR data is in the form of delta values for major diagnostic protons, given in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal standard, determined at 300 or 500 MHz using deuterated chloroform ($CDCl_3$) or DMSO-$_{d6}$ or $CD_3OD$ as solvent; conventional abbreviations for signal shape are used; for AB spectra the directly observed shifts are reported; coupling constants (J) are given in Hz; Ar designates an aromatic proton when such an assignment is made;

(viii) reduced pressures are given as absolute pressures in pascals (Pa); elevated pressures are given as gauge pressures in bars;

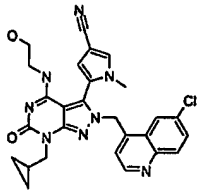
(ix) solvent ratios are given in volume:volume (v/v) terms; and

(x) Mass spectra (MS) were run using an automated system with atmospheric pressure electrospray ionization (ESI). Generally, only spectra where parent masses are observed are reported. The lowest mass major ion is reported for molecules where isotope splitting results in multiple mass spectral peaks (for example when chlorine is present).

The invention will now be illustrated by the following non-limiting examples.

**Example 1**

**5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(2-hydroxyethyl)amino]-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**



**(a) 6-Chloro-1-cyclopropylmethylpyrimidine-2,4[1H,3H]dione**

6-Chlorouracil **I** (49.64 g, 0.34 mol; Lancaster) was dissolved in anhydrous DMSO (375 mL) and treated with solid $K_2CO_3$ (23.46 g, 0.17 mol) under nitrogen. The resulting white suspension was heated to *ca.* 80 – 90 °C and kept at this temperature for 2¼ h. Foaming was observed as the temperature increased, then the reaction mixture became mostly clear. Cyclopropylmethyl bromide (65 g, 0.48 mol) was added neat *via* syringe, resulting in a white fluffy precipitate. This was followed by a catalytic amount of KI (2.88 g, 0.017 mol). The reaction mixture was heated for 19 hr, becoming mostly homogenous, then turbid with white granular precipitate, and eventually orange as the reaction progressed, remaining heterogeneous. 375 mL 1 N NaOH (aq) was added to the hot reaction mixture, causing it to darken and clear. The heat was removed and the reaction mixture allowed to cool to room temperature while stirring. It was washed with 4 x 125 mL toluene and the organic washings discarded. The aqueous phase was brought to pH 2-3 by the addition of *ca.* 100 mL conc. HCl (aq.). 50 mL water was added, and precipitation began after about one hour at room temperature; cooling in ice completed the crystallization. The yellow-green solid was collected by filtration and washed with very cold ether to remove most of the color, then dried under vacuum. Yield: 29.37 g (43%) of a light yellow solid.

**(b) 1-cyclopropylmethyl-6-hydrazinopyrimidine-2,4[1H,3H]dione**

6-Chloro-1-cyclopropylmethyluracil (24.34 g, 0.12 mol) was suspended in absolute ethanol (245 mL) under nitrogen. Anhydrous hydrazine (11.69 g, 0.36 mol) was added *via* syringe in excess, resulting in a clear yellow solution. The reaction mixture was heated at 80 – 85 °C for one hour; bright yellow crystals began forming within minutes of the application of heat. The reaction mixture was cooled to room temperature and then in an ice bath, and the crude

product collected by filtration. $N_2H_4$·xHCl was removed by trituration with cold water to give the product as a pale yellow solid, 20.47 g (86%). Mp 221 °C (dec).

**(c) 6-chloroquinoline-4-carbaldehyde [3-(cyclopropylmethyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl]hydrazone**

To a suspension of 1-cyclopropylmethyl-6-hydrazinopyrimidine-2,4[1H,3H]dione (5.05 g) in methanol (75 mL) was added 6-chloroquinoline 4- carbaldehyde (5.30 g). After stirring overnight, the reaction was filtered, yielding a yellow solid (10 g).

**(d) 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-cyclopropylmethyl-4,6-dioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

To a solution of 5-formyl-1-methyl-1*H*-pyrrole-3-carbonitrile (2.5 g) in DMF (50 mL) were added 6-chloroquinoline-4-carbaldehyde [3-(cyclopropylmethyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl]hydrazone (5.66 g) and piperdine (2 mL). After stirring overnight at $T_b$= 75 °C, the reaction was diluted with ethyl acetate and water. The organic solution was collected, washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by FlashMaster™ yielding 8.63 g of white solid. Mass: 486 $(M+H)^+$.

**(e) 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(2-hydroxyethyl)amino]-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

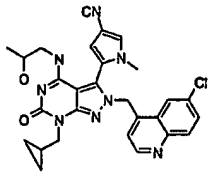
To a solution of 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-cyclopropylmethyl-4,6-dioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.42 g) in pyridine (5 mL) were added 4-chlorophenyl phosphorodichloridate (0.5 mL) and 3-nitro-1,2,4 triazole (0.15 g). After heating ($T_b$= 50 °C) for 3 h, the reaction was diluted with ethyl acetate. The organic solution was washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was dissolved in THF (10 mL) and ethanolamine (1.0 mL). After 3h, the reaction was concentrated. This residue was purified by flash chromatography using a FlashMaster™ yielding 0.22 g, ES $(M+H)^+$= 529.

Following the method of **Example 1e**, the following examples were made by reaction of 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclolpropylmethyl)-4,6-dioxo-4,5,6,7-tetrahydro-2*H*-

pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile with the appropriate amine.

**Example 2**

**5-{4-dimethylamino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

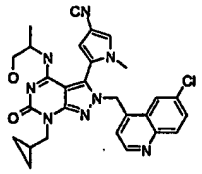


amine: 1-amino-2-propanol

1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.51 (d, *J*=5.65 Hz, 4 H) 1.16 (d, 3 H) 1.46 (m, 1 H) 3.07 (d, *J*=2.64 Hz, 2 H) 3.98 (m, 4 H) 5.12 (m, 1 H) 5.65 (d, *J*=2.45 Hz, 1 H) 6.73 (s, 1 H) 6.81 (dd, *J*=4.24, 2.54 Hz, 1 H) 7.33 (s, 1 H) 7.72 (dd, *J*=8.85, 2.26 Hz, 1 H) 7.97 (d, *J*=2.07 Hz, 1 H) 8.11 (d, *J*=9.04 Hz, 1 H) 8.82 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ = 544.

**Example 3**

**5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(2-hydroxy-1-methylethyl)amino]-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

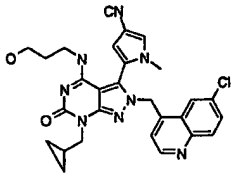


amine: 2-amino-1-propanol

ES $(M+H)^+$ = 544.

**Example 4**

**5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(3-hydroxypropyl)amino]-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**



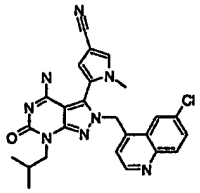
amine: 3-amino-1-propanol

1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.51 (d, *J*=5.46 Hz, 4 H) 1.48 (m, 1 H) 1.68 (m, 2 H) 3.00 (s, 3 H) 3.70 (m, 4 H) 4.00 (m, 2 H) 5.63 (s, 1 H) 5.80 (m, 1 H) 6.69 (d, *J*=1.32 Hz, 1 H) 6.77 (d, *J*=4.52 Hz, 1 H) 7.29 (m, 1 H) 7.71 (dd, *J*=9.04, 2.07 Hz, 1 H) 7.96 (d, *J*=2.07 Hz, 1 H) 8.11 (d, *J*=9.04 Hz, 1 H) 8.82 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ = 544.

Following the method of **Example 1c-e** and starting with 6-chloro-1-isobutylpyrimidine-2,4(1*H*,3*H*)-dione, the following examples were made by reaction of 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-4,6-dioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile with the appropriate amine.

**Example 5**

**5-{4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole**

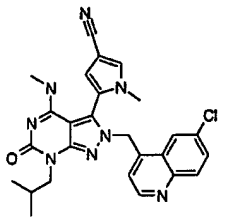


amine: ammonium hydroxide

1H NMR (500 MHz, CHLOROFORM-D) d ppm 1.00 (dd, *J*=10.40, 6.62 Hz, 6 H) 2.40 (m, 1 H) 3.02 (s, 3 H) 3.91 (d, *J*=7.57 Hz, 2 H) 5.64 (s, 2 H) 6.74 (s, 1 H) 6.77 (d, *J*=4.41 Hz, 1 H) 7.31 (d, *J*=1.26 Hz, 1 H) 7.72 (dd, *J*=9.14, 2.21 Hz, 1 H) 8.00 (d, *J*=2.21 Hz, 1 H) 8.11 (d, *J*=8.83 Hz, 1 H) 8.82 (d, *J*=4.41 Hz, 1 H); ES $(M+H)^+$ = 487.

**Example 6**

**5-{4-methylamino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

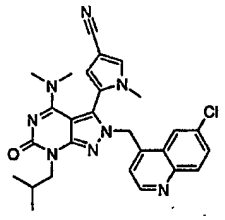


amine: methylamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 0.99 (m, 6 H) 2.44 (m, 1 H) 3.01 (m, 6 H) 3.96 (m, 2 H) 5.62 (s, 2 H) 6.73 (s, 1 H) 6.77 (d, *J*=3.47 Hz, 1 H) 7.34 (s, 1 H) 7.73 (d, *J*=8.51 Hz, 1 H) 8.00 (s, 1 H) 8.12 (d, *J*=8.83 Hz, 1 H) 8.82 (d, *J*=3.78 Hz, 1 H); ES $(M+H)^+$ = 501.

**Example 7**

**5-{4-dimethylamino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

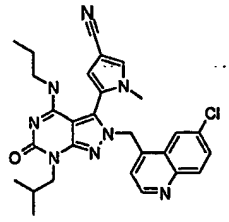


amine: dimethylamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 0.98 (m, 6 H) 2.41 (m, 1 H) 2.85 (s, 6 H) 2.99 (s, 3 H) 4.03 (m, 2 H) 5.73 (m, 1 H) 6.67 (s, 1 H) 6.74 (d, *J*=4.41 Hz, 1 H) 7.27 (m, 1 H) 7.72 (m, 1 H) 7.98 (s, 1 H) 8.12 (m, 1 H) 8.82 (d, *J*=4.10 Hz, 1 H); ES $(M+H)^+$ = 515.

**Example 8**

**5-{4-propylamino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

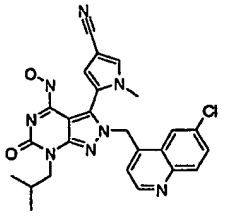


amine: propylamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 0.82 (t, *J*=7.41 Hz, 3 H) 1.01 (dd, *J*=11.35, 6.62 Hz, 6 H) 1.47 (m, 2 H) 2.44 (m, 1 H) 3.01 (s, 3 H) 3.46 (dd, *J*=22.07, 5.68 Hz, 2 H) 3.96 (m, *J*=15.45, 7.57 Hz, 1 H) 4.45 (m, 1 H) 5.63 (s, 2 H) 6.75 (d, *J*=1.58 Hz, 1 H) 6.78 (d, *J*=4.41 Hz, 1 H) 7.35 (d, *J*=1.58 Hz, 1 H) 7.73 (dd, *J*=9.14, 2.21 Hz, 1 H) 8.02 (d, *J*=2.21 Hz, 1 H) 8.12 (d, *J*=8.83 Hz, 1 H) 8.82 (d, *J*=4.10 Hz, 1 H); ES $(M+H)^+$ = 529.

**Example 9**

**5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(hydroxyamino)-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**

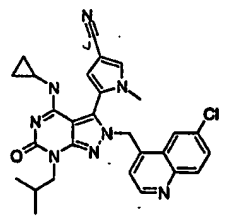


amine: hydroxylamine

1H NMR (300 MHz, DMSO-D6) d ppm 0.89 (dd, *J*=6.50, 1.98 Hz, 6 H) 2.25 (m, 1 H) 3.13 (s, 3 H) 3.68 (m, 2 H) 5.79 (m, *J*=8.85 Hz, 2 H) 6.77 (m, 1 H) 7.70 (d, *J*=1.70 Hz, 1 H) 7.80 (dd, *J*=9.04, 2.26 Hz, 1 H) 8.05 (d, *J*=9.04 Hz, 1 H) 8.14 (d, *J*=2.07 Hz, 1 H) 8.79 (d, *J*=4.33 Hz, 1 H) 9.41 (s, 1 H) 10.28 (s, 1 H); ES $(M+H)^+$ = 503

**Example 10**

**5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(cyclopropylamino)-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



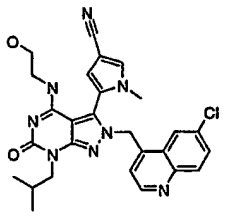
amine: cyclopropylamine

1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.83 (m, 4 H) 0.99 (m, 6 H) 2.45 (m, 1 H) 2.98 (s, 3 H) 3.83 (m, 1 H)3.96 (t, *J*=7.44 Hz, 1 H) 5.65 (m, 1 H) 6.71 (d, *J*=0.94 Hz, 1 H)

6.76 (d, *J*=4.33 Hz, 1 H) 7.33 (s, 1 H) 7.71 (m, 1 H) 7.99 (d, *J*=1.70 Hz, 1 H) 8.10 (m, 1 H) 8.81 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ = 528

**Example 11**

**5-{2-[(6-chloroquinolin-4-yl)methyl]-4-[(2-hydroxyethyl)amino]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

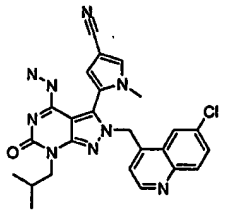


amine: ethanolamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 1.01 (dd, *J*=10.72, 6.62 Hz, 4 H) 2.43 (m, 1 H) 3.05 (s, 3 H) 3.65 (m, 4 H) 3.95 (dd, *J*=9.62, 7.72 Hz, 2 H) 5.10 (s, 1 H) 5.65 (s, 2 H) 6.73 (s, 1 H) 6.78 (d, *J*=4.41 Hz, 1 H) 7.33 (d, *J*=5.04 Hz, 1 H) 7.73 (dd, *J*=8.83, 1.89 Hz, 1 H) 8.00 (d, *J*=1.89 Hz, 1 H) 8.12 (d, *J*=8.83 Hz, 1 H) 8.82 (d, *J*=4.41 Hz, 1 H); ES $(M+H)^+$ = 531

**Example 12**

**5-{2-[(6-chloroquinolin-4-yl)methyl]-4-hydrazino-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

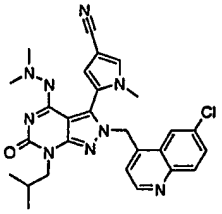


amine: hydrazine

1H NMR (300 MHz, CHLOROFORM-D) d ppm 1.00 (dd, *J*=6.50, 2.54 Hz, 6 H) 2.35 (m, *J*=13.85, 6.88 Hz, 1 H) 3.18 (m, 3 H) 3.83 (d, *J*=7.35 Hz, 3 H) 4.15 (s, 2 H) 5.65 (m, 2 H) 6.55 (d, *J*=1.13 Hz, 1 H) 6.71 (d, *J*=4.33 Hz, 1 H) 7.22 (s, 1 H) 7.70 (dd, *J*=8.85, 2.07 Hz, 1 H) 7.92 (d, *J*=1.88 Hz, 1 H) 8.10 (d, *J*=9.04 Hz, 1 H) 8.79 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ = 502

**Example 13**

**5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(2,2-dimethylhydrazino)-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



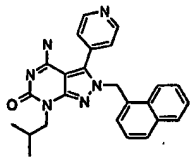
amine: dimethylhydrazine

1H NMR (300 MHz, CHLOROFORM-D) d ppm 1.01 (dd, *J*=6.59, 1.51 Hz, 4 H) 2.29 (s, 6 H) 2.36 (m, 1 H) 3.23 (s, 3 H) 3.82 (d, *J*=7.54 Hz, 1 H) 5.67 (m, 1 H) 6.54 (d, *J*=1.70 Hz, 1 H) 6.73 (d, *J*=4.52 Hz, 1 H) 7.23 (d, *J*=1.51 Hz, 1 H) 7.70 (dd, *J*=8.95, 2.17 Hz, 1 H) 7.92 (d, *J*=2.26 Hz, 1 H) 8.10 (d, *J*=9.04 Hz, 1 H) 8.80 (d, *J*=4.52 Hz, 1 H); ES $(M+H)^+$ = 531

Following the method of **Example 1**, the following examples were made by reaction of 7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione with the appropriate amine. 7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione was synthesized in analogous method to Example 1 using for step(a) 1-chloro-2-methylpropane, step (c) 1-naphthaldehyde and step (d) isonicotinaldehyde.

**Example 14**

**4-amino-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**

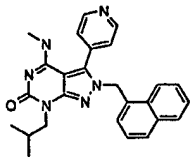


amine: ammonium hydroxide

1H NMR (500 MHz, CHLOROFORM-D) d ppm 1.01 (d, *J*=6.94 Hz, 6 H) 2.42 (m, 1 H) 3.96 (s, 2 H) 5.74 (s, 2 H) 6.76 (d, J= 7.25 Hz, 1H) 7.19 (d, *J*=5.99 Hz, 2 H) 7.31 (m, *J*=7.88 Hz, 1 H) 7.52 (m, 2 H) 7.82 (d, *J*=8.20 Hz, 1 H) 7.90 (dd, *J*=7.72, 5.20 Hz, 2 H) 8.74 (d, *J*=5.99 Hz, 2 H); ES $(M+H)^+$ = 425

**Example 15**

**7-isobutyl-4-(methylamino)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**

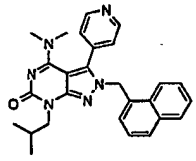


amine: methylamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 1.01 (d, *J*=6.94 Hz, 6 H) 2.46 (m, 1 H) 2.99 (d, *J*=4.73 Hz, 3 H) 4.57 (m, *J*=4.73 Hz, 1 H) 5.73 (s, 2 H) 6.76 (d, J= 7.25 Hz, 1H) 7.19 (d, *J*=5.99 Hz, 2 H) 7.31 (m, *J*=7.88 Hz, 1 H) 7.52 (m, 2 H) 7.82 (d, *J*=8.20 Hz, 1 H) 7.90 (dd, *J*=7.72, 5.20 Hz, 2 H) 8.74 (d, *J*=5.99 Hz, 2 H); ES $(M+H)^+$ = 439.

**Example 16**

**4-(dimethylamino)-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**

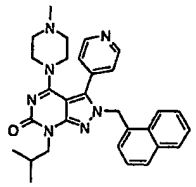


amine: dimethylamine

1H NMR (500 MHz, CHLOROFORM-D) d ppm 1.00 (d, *J*=6.62 Hz, 6 H) 2.43 (m, 1 H) 2.78 (s, 6 H) 4.01 (d, *J*=7.57 Hz, 2 H) 5.72 (s, 2 H) 6.75 (d, *J*=6.94 Hz, 1 H) 7.17 (d, *J*=4.73 Hz, 1 H) 7.35 (t, *J*=7.72 Hz, 1 H) 7.54 (m, 2 H) 7.83 (d, *J*=8.20 Hz, 1 H) 7.89 (dd, *J*=14.03, 8.04 Hz, 2 H) 8.66 (s, 2 H); ES $(M+H)^+$ = 453.

**Example 17**

**7-isobutyl-4-(4-methylpiperazin-1-yl)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**

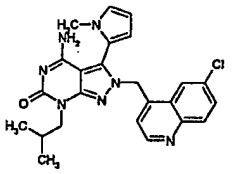


amine: 1-methylpiperazine

1H NMR (500 MHz, DMSO-D6) d ppm 1.01 (d, *J*=6.94 Hz, 6 H) 2.19 (s, 3 H) 2.43 (m, 1 H) 3.35 (s, 4 H) 4.01 (d, *J*=7.57 Hz, 2 H) 5.74 (s, 2 H) 6.77 (d, *J*=6.94 Hz, 1 H) 7.18 (m, 2 H) 7.36 (m, 1 H) 7.53 (m, 2 H) 7.83 (d, *J*=8.51 Hz, 1 H) 7.89 (dd, *J*=15.29, 8.04 Hz, 2 H) 8.69 (d, *J*=5.99 Hz, 2 H); ES $(M+H)^+$ = 508.

**Example 18**

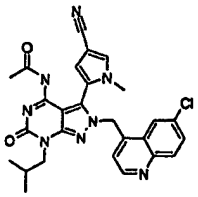
**4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-3-(1-methyl-1*H*-pyrrol-2-yl)-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**



4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-3-(1-methyl-1*H*-pyrrol-2-yl)-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one was synthesized in analogous method to Example 1 using for step (a) 1-chloro-2-methylpropane and for step (d) 1-methyl-1*H*-pyrrole-2-carbaldehyde. 1H NMR (500 MHz, CHLOROFORM-D) d ppm 0.99 (dd, *J*=9.14, 6.62 Hz, 6 H) 2.33 (m, 1 H) 3.33 (s, 3 H) 3.90 (m, 2 H) 5.71 (d, *J*=15.76 Hz, 1 H) 5.87 (d, *J*=15.45 Hz, 1 H) 6.46 (m, 1 H) 7.08 (m, 1 H) 7.86 (dd, *J*=8.83, 1.89 Hz, 1 H) 8.04 (d, *J*=1.89 Hz, 1 H) 8.31 (d, *J*=9.14 Hz, 1 H) 9.01 (d, *J*=4.73 Hz, 1 H) 12.66 (s, 1 H); ES $(M+H)^+$ 462.

**Example 19**

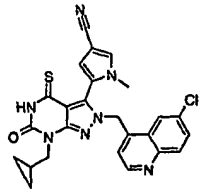
***N*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl]acetamide**



To a solution of 5-{4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.15g) in pyridine (3 mL) was added acetic anhydride (0.15 mL). After stirring at rtfor 4 h, the reaction was concentrated and purified by Flash Master (0.072 g). 1H NMR (300 MHz, CHLOROFORM-D) d ppm 1.00 (m, 6 H) 2.08 (m, 3 H) 2.39 (m, 1 H) 3.24 (s, 3 H) 3.91 (d, *J*=7.72 Hz, 2 H) 5.75 (m, 2 H) 6.61 (d, *J*=1.70 Hz, 1 H) 6.78 (d, *J*=4.33 Hz, 1 H) 7.30 (d, *J*=1.70 Hz, 1 H) 7.72 (dd, *J*=9.04, 2.26 Hz, 1 H) 7.89 (d, *J*=2.07 Hz, 1 H) 8.12 (d, *J*=8.85 Hz, 1 H) 8.83 (d, *J*=4.52 Hz, 1 H) 12.28 (s, 1 H); ES (M+H)+ 529.

**Example 20**

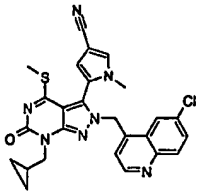
**5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



To a solution of 5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclolpropylmethyl)-4,6-dioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.50 g) in pyridine (10 mL) was added $P_4S_{10}$ (0.72 g). After heating ($T_b$= 110 C) overnight, the reaction was concentrated. The residue was dissolved in EtOAc and water. The organic solution was collected, washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by first by flash chromatography using a FlashMaster™ yielding 0.14 g, 1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.56 (m, 4 H) 1.47 (m, 1 H) 3.05 (s, 3 H) 3.97 (m, 2 H) 5.70 (m, 2 H) 6.64 (d, *J*=1.70 Hz, 1 H) 6.79 (d, *J*=4.33 Hz, 1 H) 7.72 (dd, *J*=9.04, 2.26 Hz, 1 H) 7.94 (d, *J*=2.07 Hz, 1 H) 8.12 (d, *J*=9.04 Hz, 1 H) 8.84 (d, *J*=4.33 Hz, 1 H) 9.12 (s, 1 H); ES M+H$^+$= 503.

**Example 21**

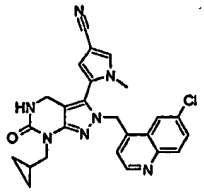
**5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-(methylthio)-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



To a solution of 5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile (0.33 g) in THF (5 mL) were added iodomethane( 0.10 mL) and 1,8-diazabicycl[4.3.0]undec-7-ene (0.15 mL). After 2 h, the reaction was diluted with ethyl acetate and water. The slurry was filtered and washed with water to yield 250 mg product. 1H NMR (300 MHz, DMSO-D6) d ppm 0.56 (d, *J*=5.46 Hz, 4 H) 1.28 (m, 1 H) 2.55 (s, 3 H) 2.95 (s, 3 H) 4.07 (dd, *J*=7.25, 4.80 Hz, 2 H) 5.69 (d, *J*=2.45 Hz, 2 H) 6.71 (d, *J*=1.70 Hz, 1 H) 6.79 (d, *J*=4.52 Hz, 1 H) 7.29 (m, 1 H) 7.72 (dd, *J*=9.04, 2.26 Hz, 1 H) 7.99 (d, *J*=2.26 Hz, 1 H) 8.11 (d, *J*=9.04 Hz, 1 H) 8.83 (d, *J*=4.33 Hz, 1 H); ES $M+H^+$= 516.

**Example 22**

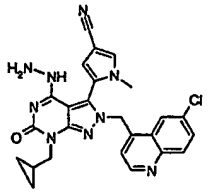
**5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



To a solution of 5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile (0.17 g) in methanol (1 mL) and THF (1.5 mL) was added $NiCl_2$-$6H_2O$ ( (0.11g). After the nickel had dissolved, sodium borohyride (0.5 g) was added. After 30 min., the reaction was concentrated. The residue was diluted with ethyl acetate and water. The organic solution was washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by flash chromatography using a FlashMaster™ yielding 44 mg, 1H NMR (300 MHz, DMSO-D6) d ppm 0.34 (m, 4 H) 1.23 (m, 1 H) 3.19 (s, 3 H) 3.57 (d, *J*=6.97 Hz, 2 H) 4.15 (s, 2 H) 5.63 (s, 2 H) 6.68 (d, *J*=1.70 Hz, 1 H) 6.76 (d, *J*=4.33 Hz, 1 H) 6.90 (s, 1 H) 7.72 (d, *J*=1.70 Hz, 1 H) 7.79 (dd, *J*=9.04, 2.26 Hz, 1 H) 8.05 (d, *J*=8.85 Hz, 1 H) 8.17 (d, *J*=2.07 Hz, 1 H) 8.80 (d, *J*=4.52 Hz, 1 H); ES $M+H^+$= 472.

**Example 23**

**5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-hydrazino-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**

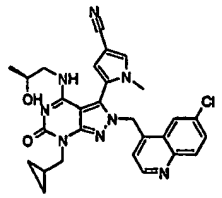


To a solution of 5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile (03.0 g) in acetonitrile (5 mL) were added hydrazine hydrate (0.50 mL) and mercury(II) chloride (250 mg). After 5 h, the reaction was diluted with ethyl acetate and filtered through a celite bed. The residue was purified by flash chromatography using a FlashMaster™ yielding 120 mg, 1H NMR (300 MHz, DMSO-D6) d ppm 0.44 (m, 4 H) 1.34 (m, 1 H) 3.17 (m, 3 H) 3.80 (m, *J*=6.97, 6.97 Hz, 2 H) 5.60 (q, *J*=15.89 Hz, 2 H) 6.48 (d, *J*=1.70 Hz, 1 H) 6.71 (d, *J*=4.52 Hz, 1 H) 7.22 (d, *J*=1.51 Hz, 1 H) 7.66 (dd, *J*=9.04, 2.07 Hz, 1 H) 7.85 (d, *J*=2.07 Hz, 1 H) 8.02 (d, *J*=9.04 Hz, 1 H) 8.71 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$= 500.

Following the method of **Example 23**, the following examples were made by reaction of 5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile with the appropriate amine.

**Example 24**

**5-(2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-{[(2*S*)-2-hydroxypropyl]amino}-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)-1-methyl-1*H*-pyrrole-3-carbonitrile**

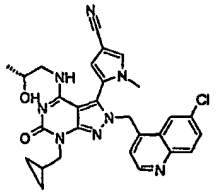


amine: (S)-(+)-1-amino-2-propanol

1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.50 (d, *J*=4.52 Hz, 4 H) 1.16 (dd, *J*=6.22, 1.88 Hz, 3 H) 1.46 (m, 1 H) 2.50 (m, 1 H) 3.08 (d, *J*=3.01 Hz, 3 H) 3.89 (m, 2 H) 3.99 (m, *J*=6.78, 6.78 Hz, 1 H) 5.24 (m, 1 H) 5.66 (d, *J*=2.07 Hz, 2 H) 6.73 (d, *J*=1.70 Hz, 1 H) 6.81 (dd, *J*=4.24, 2.35 Hz, 1 H) 7.34 (s, 1 H) 7.72 (dd, *J*=8.85, 2.07 Hz, 1 H) 7.96 (d, *J*=2.26 Hz, 1 H) 8.12 (d, *J*=8.85 Hz, 1 H) 8.83 (d, *J*=4.52 Hz, 1 H); ES $(M+H)^+$= 544

**Example 25**

**5-(2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-{[(2*R*)-2-hydroxypropyl]amino}-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)-1-methyl-1*H*-pyrrole-3-carbonitrile**

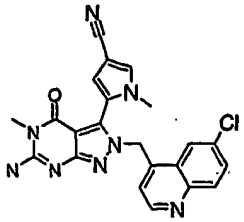


amine: (R)-(-1)-1-amino-2-propanol

1H NMR (300 MHz, DMSO-D6) d ppm 0.51 (d, *J*=5.46 Hz, 4 H) 1.17 (m, 3 H) 1.47 (m, 1 H) 3.07 (d, *J*=3.20 Hz, 3 H) 3.96 (m, 2 H) 3.99 (m, 2 H) 5.18 (s, 1 H) 5.66 (d, *J*=2.45 Hz, 2 H) 6.73 (d, *J*=1.70 Hz, 1 H) 6.81 (dd, *J*=4.14, 2.45 Hz, 1 H) 7.33 (s, 1 H) 7.72 (dd, *J*=9.04, 2.07 Hz, 1 H) 7.96 (d, *J*=2.26 Hz, 1 H) 8.11 (d, *J*=9.04 Hz, 1 H) 8.83 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$= 544

**Example 26**

**5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**



**(a) 2-amino-6-chloropyrimidin-4(3*H*)-one**

2-Amino-4,6-dichloropyrimidine (10.6 g) was suspended in 1N NaOH (100 mL) and heated to reflux. Additional $NaOH_{(s)}$ (1.0 g) was added after 2 h and 4 h. After 5h, the solution was

cooled with an ice bath and neutralized with acetic acid. The white precipitate was filtered, washed with water, and dried on a high vacuum to yield 9.28 g of white solid.

**(b) 2-amino-6-chloro-3-methylpyrimidin-4(3*H*)-one**

To a suspension of 2-amino-6-chloropyrimidin-4(3*H*)-one (5.37 g) in ethanol (300 mL) was added $NaOH_{(s)}$ (1.94 g) and heated ($T_b$= 60 °C). After 30 min., iodomethane (3.0 mL) was added and the reaction heated to reflux. After 2h, additional $NaOH_{(s)}$ (2.36 g) and iodomethane (1.5 mL) were added. After 7 h, the reaction was concentrated. The residue was diluted with water and neutralized with acetic acid. The resulting solid was collected by filtration yielding 2.43 g white solid after drying on high vacuum.

**(c) 2-amino-6-hydrazino-3-methylpyrimidin-4(3*H*)-one**

To a suspension of 2-amino-6-chloro-3-methylpyrimidin-4(3*H*)-one (2.43 g) in ethanol was added hydrazine hydrate (12.0 mL). After 7 h at reflux, the suspension was cooled, filtered and dried on high vacuum yielding 1.01 g of white solid.

**(d) 6-chloroquinoline-4-carbaldehyde (2-amino-1-methyl-6-oxo-1,6-dihydropyrimidin-4-yl)hydrazone**

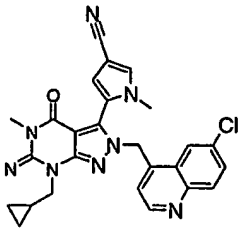
To a suspension of 2-amino-6-hydrazino-3-methylpyrimidin-4(3*H*)-one (1.01 g) in methanol (20 ml) was added 6-chloroquinoline 4- carbaldehyde (1.35 g). After 3h, the reaction was filtered yielding a yellow solid (2.14 g).

**(e) 5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile**

To a suspension of 6-chloroquinoline-4-carbaldehyde (2-amino-1-methyl-6-oxo-1,6-dihydropyrimidin-4-yl)hydrazone (2.14 g) in DMF (25 mL) were added 5-formyl-1-methyl-1*H*-pyrrole-3-carbonitrile (0.86 g) and piperdine (0.50 mL). After stirring overnight at $T_b$= 60 °C, the solution was diluted with ethylacetate and water. The organic solution was collected, washed with sat'd $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was suspended in methanol and filtered (1.34 g). 1H NMR (300 MHz, DMSO-D6) d ppm 2.50 (m, 3 H) 3.28 (d, *J*=4.33 Hz, 6 H) 5.87 (m, 2 H) 6.74 (d, *J*=1.70 Hz, 1 H) 6.79 (d, *J*=4.33 Hz, 1 H) 6.94 (s, 2 H) 7.79 (m, 2 H) 8.07 (m, 2 H) 8.80 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ 445.

**Example 27**

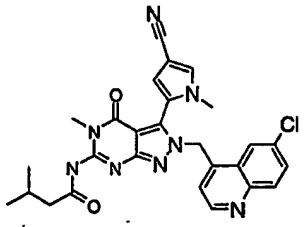
**5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-imino-5-methyl-4-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**



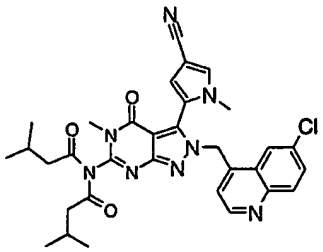
To a suspension of 5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.12 g) in THF (2 mL) and 1,8-diazabicyclo[4.3.0]undec-7-ene (0.10 mL) was added (bromomethyl)cyclopropane (0.10 mL). The reaction was heated in a microwave for 1h at 140 °C. The reaction was then concentrated and purified by FlashMaster™ yielding 58 mg of brown foam. 1H NMR (300 MHz, DMSO-D6) d ppm 0.53 (m, 4 H) 1.40 (m, 1 H) 3.33 (s, 3 H) 3.39 (s, 3 H) 3.98 (m, 2 H) 5.68 (m, 1 H) 6.56 (d, *J*=1.70 Hz, 1 H) 6.81 (d, *J*=4.33 Hz, 1 H) 7.31 (d, *J*=1.51 Hz, 1 H) 7.71 (dd, *J*=9.04, 2.07 Hz, 1 H) 7.84 (d, *J*=2.07 Hz, 1 H) 8.12 (d, *J*=8.85 Hz, 1 H) 8.83 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ 499.

**Example 28-29**

***N*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl]-3-methylbutanamide**



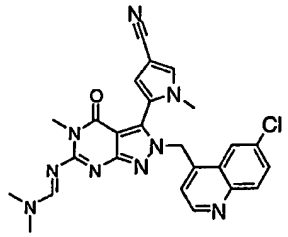
***N,N*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl]-bis-3-methylbutanamide**



To a solution of 5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.11 g) in THF (5 mL) and triethylamine (0.50 mL) was added isovaleryl chloride (0.05 mL). After stirring overnight, DMF (1.0 mL), 1,8-diazabicyclo[4.3.0]undec-7-ene (0.10 mL) and additional isovaleryl chloride (0.05 mL) were added. After 5 h additional, the reaction was warmed ($T_b$= 55 °C). After stirring overnight again, the reaction was then concentrated and purified by FlashMaster™ yielding two products: mono-acylated *N*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl]-3-methylbutanamide (52 mg) 1H NMR (300 MHz, CHLOROFORM-D) d ppm 1.01 (m, 6 H) 2.24 (m, 1 H) 2.40 (m, *J*=6.97 Hz, 2 H) 3.39 (s, 3 H) 3.50 (s, 3 H) 5.76 (dd, *J*=70.64, 15.64 Hz, 2 H) 6.60 (m, 1 H) 6.93 (d, *J*=1.51 Hz, 1 H) 7.36 (s, 1 H) 7.64 (m, 1 H) 7.71 (dd, *J*=9.04, 2.07 Hz, 1 H) 8.12 (d, *J*=9.23 Hz, 1 H) 8.86 (d, *J*=4.33 Hz, 1 H) 14.38 (s, 1 H); ES $(M+H)^+$ 529 and bis-acylated *N,N*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl]-bis-3-methylbutanamide (49 mg) 1H NMR (300 MHz, CHLOROFORM-D) d ppm 0.95 (m, 12 H) 2.19 (m, 4 H) 2.65 (m, 2 H) 3.40 (m, 6 H) 5.90 (dd, *J*=81.01, 15.26 Hz, 1 H) 6.67 (d, *J*=1.70 Hz, 1 H) 7.06 (d, *J*=4.52 Hz, 1 H) 7.39 (d, *J*=1.51 Hz, 1 H) 7.63 (d, *J*=2.07 Hz, 1 H) 7.71 (dd, *J*=8.95, 2.17 Hz, 1 H) 8.12 (d, *J*=9.04 Hz, 1 H) 8.86 (d, *J*=4.52 Hz, 1 H); ES $(M+H)^+$ 613

**Example 30**

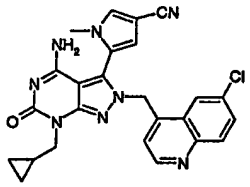
***N'*-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1*H*-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl]-*N,N*-dimethylimidoformamide**



To a suspension of 5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl}-1-methyl-1*H*-pyrrole-3-carbonitrile (0.12 g) in DMF (3 mL) and 1,8-diazabicyclo[4.3.0]undec-7-ene (0.20 mL) was added propanesulfonyl chloride (0.10 mL). After stirring overnight at rt, the solution was diluted with ethyl acetate and water. The organic solution was collected, washed with sat'd $NaHCO_3$ and brine, dried ($Na_2SO_4$), filtered and concentrated. The reaction was then concentrated and purified by FlashMaster™ yielding 65 mg of brown foam. 1H NMR (300 MHz, CHLOROFORM-D) d ppm 3.19 (d, *J*=9.98 Hz, 6 H) 3.45 (s, 3 H) 3.58 (s, 3 H) 5.80 (dd, *J*=77.14, 15.73 Hz, 2 H) 6.54 (d, *J*=1.70 Hz, 1 H) 7.00 (d, *J*=4.52 Hz, 1 H) 7.34 (d, *J*=1.70 Hz, 1 H) 7.69 (m, 2 H) 8.10 (m, 1 H) 8.78 (s, 1 H) 8.82 (d, *J*=4.33 Hz, 1 H); ES $(M+H)^+$ 500.

**Example 31**

**5-[4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile**

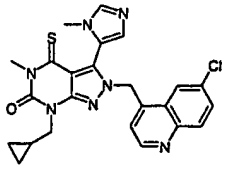


5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile (0.5g, 1.0 mmol) was dissolved in 10 mL anhydrous THF. Anhydrous ammonia in methanol (20 mL of 2M solution) was added, followed by mercury (II) chloride (410 mg, 1.5 mmol, 1.5 eq). The mixture was heated to 60°C for 48h. Volatiles were evaporated and the residue dissolved in 100 mL ethylacetate, 50 mL dichloromethane, and 100 mL water. The organic layer was washed with water (100 mL) and dried over sodium sulfate. The residue was purified by chromatography on silica (gradient: dichloromethane to 10% methanol in dichloromethane), yielding 232 mg (48%) of the product as a yellow solid. ES $M+H^+ = 485$. $^1H$ NMR (300MHz, DMSO-$d_6$): 8.80 (d, J = 6Hz, 1H); 8.16 (d, J = 3Hz, 1H); 8.06 (d, J = 9Hz, 1H); 7.80 (m,

2H); 6.85 (d, J = 3Hz, 1H); 6.81 (d, J = 6Hz, 1H); 5.87 (d, J =16Hz, 1H); 5.72 (d, J = 16Hz, 1H); 3.77 (m, 2H); 3.33 (s, 3H); 1.28 (m, 1H); 0.45-0.3 (m, br, 4H).

**Example 32**

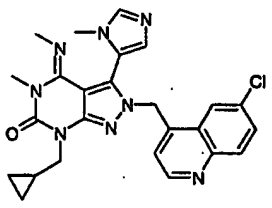
**2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-thioxo-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**



2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (250 mg, 0.53 mmol) and P4S10 (470 mg, 1.06 mmol, 2.0 eq.) were stirred in 5 mL anhydrous pyridine. The mixture was heated in a microwave reactor at 150°C for 2h. 15 min. The reaction was diluted with 50 mL ethylacetate and 50 mL water. The aqueous layer was washed 2x30 mL with ethylacetate. The combined organic layers were washed with water (70 mL) and brine (50 mL) and dried over sodium sulfate. Volatiles were removed under vacuum and the residue purified by chromatography on silica (gradient: dichloromethane to 10% methanol in dichloromethane). Yield 40 %. ES+H$^+$ = 492. $^1$H NMR (300MHz, DMSO-$d_6$) 8.82 (d, J = 3Hz, 1H); 8.59 (d, J = 6Hz, 1H); 8.16 (d, J = 2Hz, 1H); 7.80 (s, 1H); 7.38 (m, 1H); 7.03 (s, 1H); 6.80 (d, J = 6Hz, 1H); 5.90 (m, 2H); 3.90 (m, 2H); 3.67 (s, 3H); 3.16 (s, 3H); 1.40 (m, 1H); 0.5-0.4 (m, 4H).

**Example 33**

**(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-(methylimino)-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one**



2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-thioxo-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one (210 mg, 0.43 mmol) was dissolved in 5 mL anhydrous THF. Methylamine (4 eq as 2.0 M solution in THF) added,

and the solution heated to 60 °C. Mercury (II) chloride ( 232 mg, 0.86mmol, 2 eq.) was added and the solution stirred at 60 °C for one hour. As no reaction was evident (as judged by LC/MS of an aliquot), another 4 eq. amine was added, and the reaction heated to 110°C for one hour in the microwave reactor. The reaction mixture was diluted with 25 mL ethylacetate and filtered through celite. The celite was washed with small amount of solvent. The organic layer was washed with water (50 mL) and brine (50 mL), and dried over sodium sulfate. The volatiles were removed under vacuum and the residue purified by chromatography on silica (gradient: dichloromethane to 10% methanol in dichloromethane). Yield 35 %. ES+$H^+$ = 489. $^1$H NMR (300MHz, $CDCl_3$) 8.75 (d, J = 6Hz, 1H); 8.04 (d, J = 9Hz, 1H); 7.96 (d, J = 2Hz, 1H); 7.64 (dd, J = 9Hz, 2Hz, 1H); 7.52 (s, 1H); 7.20 (s, 1H); 6.65 (d, J = 6Hz, 1H); 5.63 (m, 2H); 3.87 (m, 2H); 3.31 (s, 3H); 2.98 (s, 3H); 2.66 (s, 3H); 1.37 (m, 1H); 0.5-0.41 (m, 4H).

**Utility**

The compounds of the present invention have utility for the prevention and treatment of *H. pylori* infection. Methods of treatment target the prevention of cell wall biosynthesis through the MurI enzyme. Compounds that inhibit MurI activity control the production of cell wall biosynthesis. The inhibition of MurI will inhibit growth of *H. pylori* and will reduce or prevent the diseases resulting from *H. pylori* infection such as peptic ulcers, gastritis and MALT lymphoma. The compounds of the present invention have utility for the prevention and treatment of such disorders.

Compounds of the present invention have been shown to inhibit MurI, as determined by glutamate racemase activity assay described herein.

Compounds provided by this invention should also be useful as standards and reagents in determining the ability of a potential pharmaceutical to inhibit MurI. These would be provided in commercial kits comprising a compound of this invention.

**Abbreviations**

As used herein "rt" denotes room temperature, "ug " denotes microgram, "mg" denotes milligram, "g" denotes gram, "uL" denotes microliter, "mL" denotes milliliter, "L" denotes

liter, "nM" denotes nanomolar, "uM" denotes micromolar, "mM" denotes millimolar, "M" denotes molar, "nm" denotes nanometer, "DMSO" denotes dimethyl sulfoxide, "DTT" denotes dithiothreitol, "EDTA" denotes ethylenediaminetetraacetate,

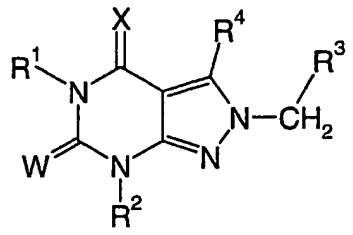
Assay

**Glutamate Racemase Activity Assay:**

Glutamate racemase (MurI) activity was assayed by measuring the conversion of glutamate from D to L enantiomer. This reaction was coupled to the reduction of $NAD^+$ to NADH by L-glutamate dehydrogenase (LGDH). LGDH from bovine liver was obtained as a lyophilized powder (Sigma #G-7882) and dissolved in 10 mM Tris (Sigma #T-6791), pH 7.5, buffer containing 0.1 mM EDTA (Fisher #BP118-500) and 50% glycerol (Sigma #G-9012). The assay mixture consisted of 100 mM Tris-HCl, pH 8.0, 10 mM β-NAD (Sigma #N-7004), 5 mM DTT (Sigma #D-5545), 0.03% PEG (mw 8000, Sigma #P-5413), 0.03 mg/mL BSA (Pierce #23210), 15 U/mL LGDH, D-glutamate (40 μM, Fluka #49460), and purified MurI (1 uM). The assay was performed in 96-well black microtiter plates (Greiner #XN2-9511) with a final assay volume of 100 μL. Compounds were prepared as 20 mM stock solutions in dimethyl sulfoxide (DMSO, Sigma #D-5879) and serial dilutions were prepared from these solutions using DMSO, 2 μL of which were added to the wells. Activity at room temperature was measured by monitoring the increase in fluorescence using a TECAN Ultra plate reader with 340 nm excitation and 465 nm emission filters. The compounds provided have measured IC50 of less then 400 μM

Claims:

1. A compound having the structural formula (I):



(I)

wherein,

X is S, O, or $NR^{20}$, provided that when W is O, then X is not O,

X and the double bond to which it is attached can be replaced with 2 hydrogen atoms,

W is S, O, or $NR^{20}$; provided that when X is O, then W is not O;

$R^1$ is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, hydroxy, amino, or optionally substituted heterocycle;

$R^2$ is H, optionally substituted alkyl, optionally substituted alkylcycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, or optionally substituted heterocycle;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3

or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal $-OC_{1-2}haloalkylO-$, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}alkyl$, $C_{1-6}haloalkyl$, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}alky$, $-NC_{1-6}alkyl$, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}alkyl$, $-NC_{1-6}alkyl$, $-N(C_{1-6}alkyl)$ are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}alkyl$ wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}haloalkyl$, $-OC_{1-6}haloalkyl$, $C_{1-6}alkyl$, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^a$ is, independently at each instance, H, $C_{1-6}alkyl$, $-C(=O)C_{1-4}alkyl$, $C_{1-4}haloalkyl$, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, -$OC(=O)R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, NH($C_{1-4}$ alkyl), N($C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

or a pharmaceutically acceptable salt thereof.

2. A compound as recited in Claim 1 wherein:

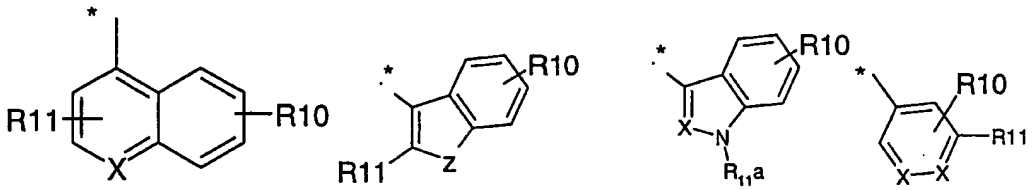
$R^1$ is H, or $C_{1-6}$alkyl, or –$(CH_2)_n$cycloalkyl or –$(CH_2)_{1-2}$Het wherein $C_{1-6}$alkyl or –$(CH_2)_n$cycloalkyl or –$(CH_2)_{1-2}$Het is optionally substituted by 1, 2 or 3 substituents selected from Het, halogen, -CN, -$OR^a$, -$NR^aR^a$, -$C(=O)OR^a$, -$C(=O)NR^aR^a$, -$OC(=O)C_{1-4}$alkyl, -$S(=O)_nR^c$, -$S(=O)_nNR^aR^a$ or -$NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

3. A compound as recited in Claim 1 wherein:

$R^2$ is –$(CH_2)_{1-3}$cycloalkyl or -$C_{1-12}$alkyl wherein –$(CH_2)_{1-3}$cycloalkyl or -$C_{1-12}$alkyl is optionally substituted with 0, 1, 2 or 3 substituents selected from Het, $S(=O)_nR^c$, -$S(=O)_nNR^aR^a$ halogen, -CN, -$OR^a$, -$NR^aR^a$, -$C(=O)OR^a$, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$OC(=O)C_{1-4}$alkyl, or -$NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

4. A compound as recited in Claim 1 wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

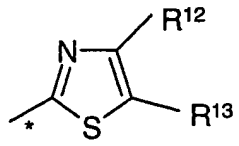



(i) (ii) (iii) (iv)

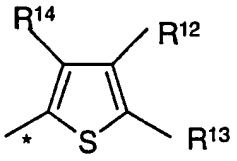
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

5. A compound as recited in Claim 1 wherein:

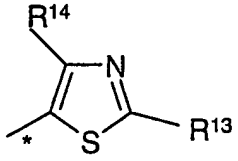
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



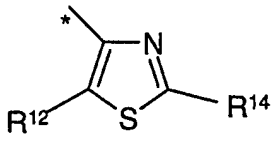

(a)



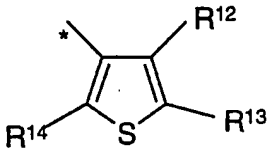

(b)



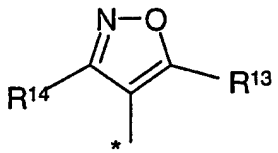

(c)



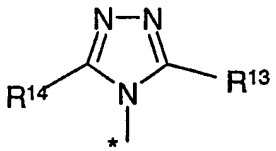

(d)



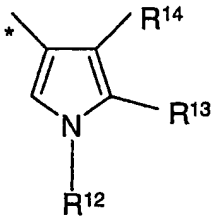

(e)



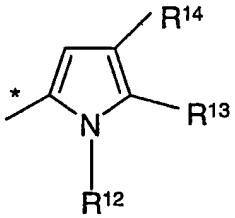

(f)



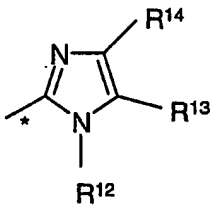

(g)



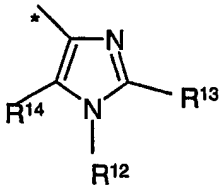

(h)



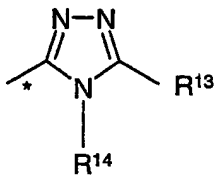

(i)



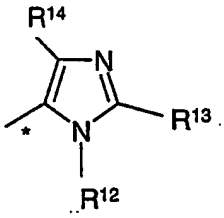

(j)



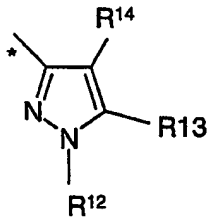

(k)



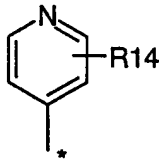

(l)



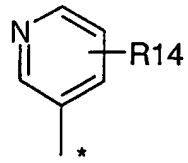

(m)



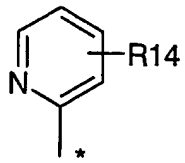

(n)



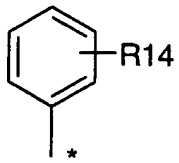

(o)



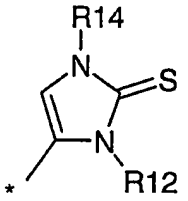

(p)



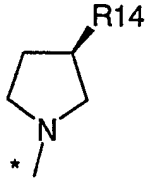

(q)



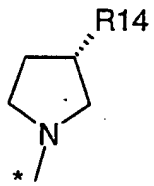

(r)



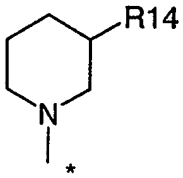

(s)



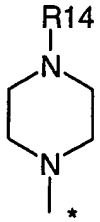

(t)



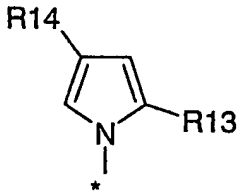

(u)



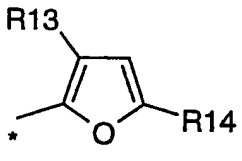

(v)



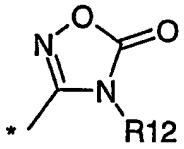

(w)



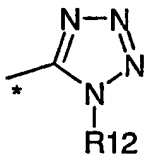

(x)



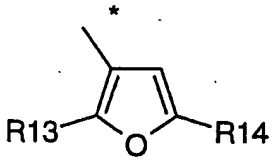

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

6. A compound as recited in Claim 1 wherein:

X is S, O, or $NR^{20}$, provided that when W is O, then X is not O; or X and the double bond to which it is attached can be 2 hydrogen atoms,

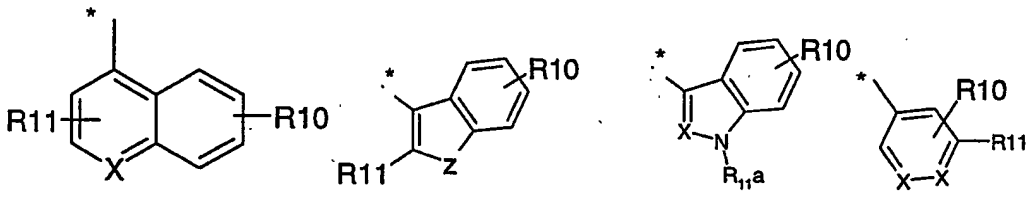
W is S, O, or $NR^{20}$; provided that when X is O, then W is not O;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

$R^2$ is $-CH_2CH_2CH_3$, $-CH_2$-cyclopropyl, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2F$, $-CH_2$-cyclobutyl, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2$-methylphenyl, $-CH_2$-phenol, $-CH_2$-(3,5-dimethylisoxazol-4-yl), $-CH_2$-S-phenyl, $-CH_2$-phenylcarboxyl, or $-CH_2SCF_3$;

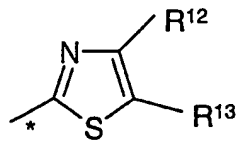
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



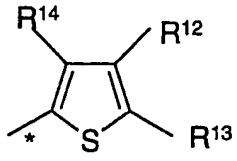

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

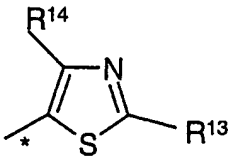
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



(a)



(b)



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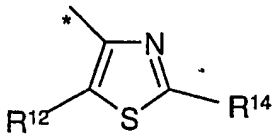
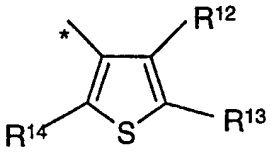
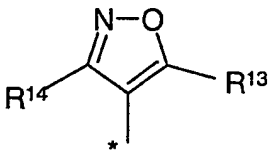


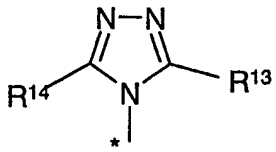
(d)



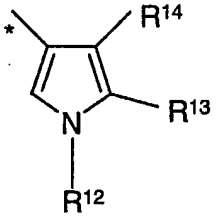
(e)



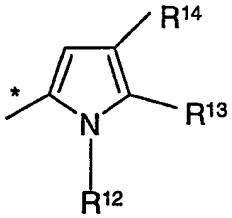
(f)



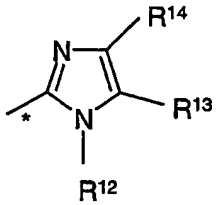
(g)



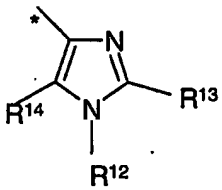
(h)



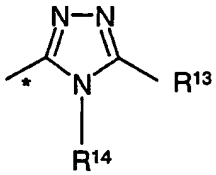
(i)



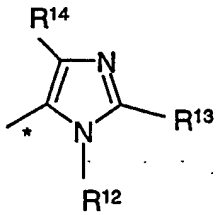
(j)



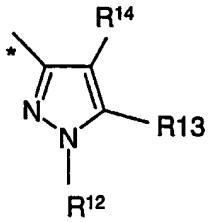
(k)



(l)



(m)



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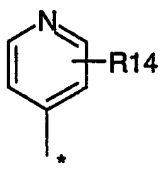
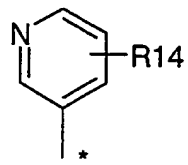
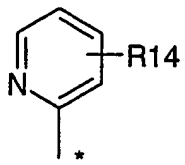


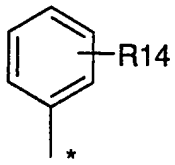
(o)



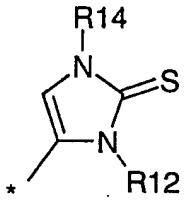

(p)




(q)




(r)

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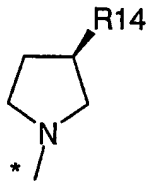
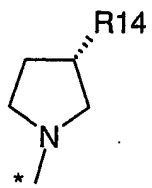
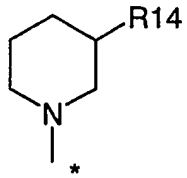


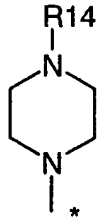

(t)



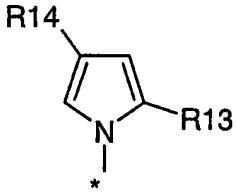

(u)



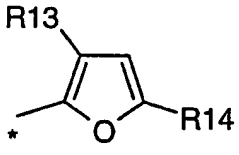

(v)



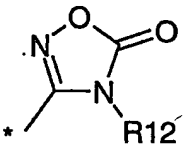

(w)



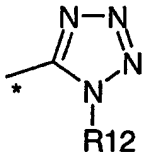

(x)



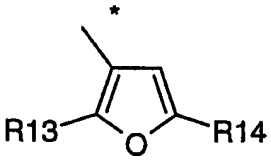

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

7. A compound of formula (I) selected from:

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-thioxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-imino-5-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4-(methylimino)-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-imino-5-methyl-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4-oxo-6-thioxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-6-(methylimino)-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

N-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]acetamide;

N-[(6Z)-2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]methanesulfonamide;

5-((6Z)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-{[2-(dimethylamino)ethyl]imino}-5-methyl-4-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)-1-methyl-1H-pyrrole-3-carbonitrile;

N~1~-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-(cyclopropylmethyl)-5-methyl-4-oxo-2,4,5,7-tetrahydro-6H-pyrazolo[3,4-d]pyrimidin-6-ylidene]-N~2~,N~2~-dimethylglycinamide;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

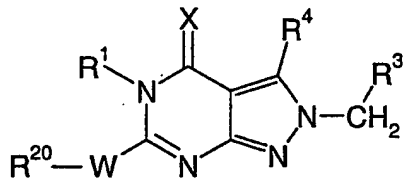
5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-thioxo-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one;

(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-3-(1-methyl-1*H*-imidazol-5-yl)-4-(methylimino)-2,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*d*]pyrimidin-6-one.

8. A compound having the structural formula (II):



(II)

wherein,

X is S, O, or $NR^{20}$,

X and the double bond to which it is attached can be replaced with 2 hydrogen atoms,

W is S, O, or $NR^{21}$;

$R^1$ is H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, hydroxy, amino, or optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, $-OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, -

$C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl$)_2$, $C_{1-4}$ alkanoylamino, $(C_{1-4}$ alkanoyl$)_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl$)_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)$S(O)_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{21}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$; optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein the substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl$)_2$, $C_{1-4}$ alkanoylamino, $(C_{1-4}$ alkanoyl$)_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl$)_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)$S(O)_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -$C(=O)NR^aR^a$, -$C(=O)OR^a$, -$NR^aC(=O)R^a$, -$OC(=O)R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

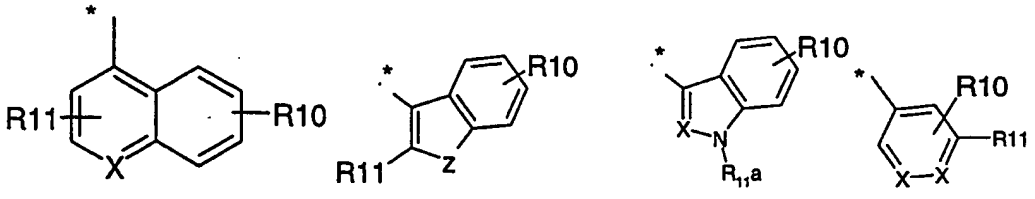
or a pharmaceutically acceptable salt thereof.

9. A compound as recited in Claim 8 wherein:

$R^1$ is H, or $C_{1-6}$alkyl, or –$(CH_2)_n$cycloalkyl wherein $C_{1-6}$alkyl or –$(CH_2)_n$cycloalkyl is optionally substituted by 1, 2 or 3 substituents selected from Het, halogen, -CN, -$OR^a$, -$NR^aR^a$, -$C(=O)OR^a$, -$C(=O)NR^aR^a$, -$OC(=O)C_{1-4}$alkyl or -$NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

10. A compound as recited in Claim 8 wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

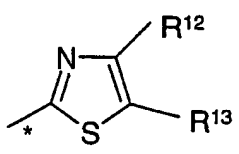



(i) (ii) (iii) (iv)

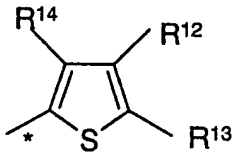
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

11. A compound as recited in Claim 8 wherein:

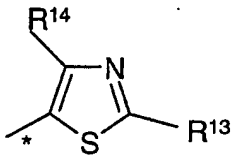
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



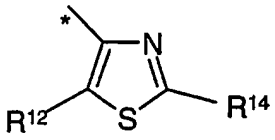
(a)



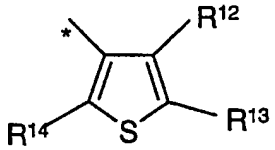
(b)



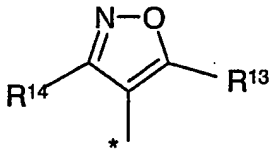
(c)



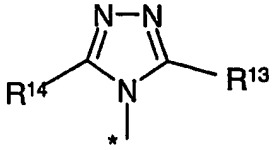
(d)



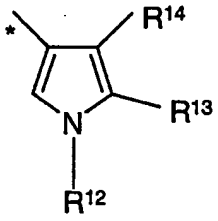
(e)



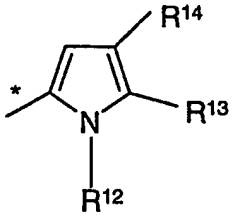
(f)



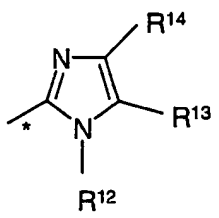
(g)



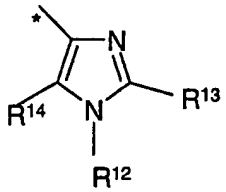
(h)



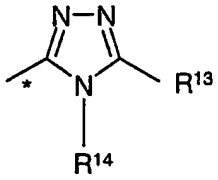
(i)



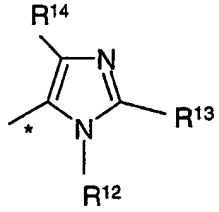

(j)



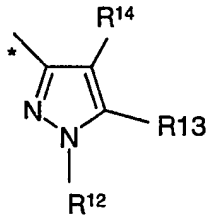

(k)



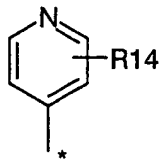

(l)



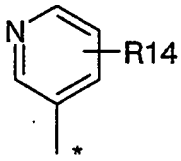

(m)



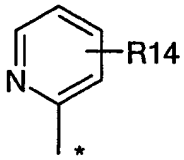

(n)



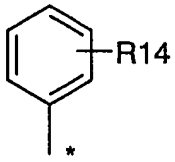

(o)



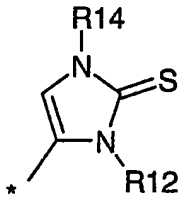

(p)



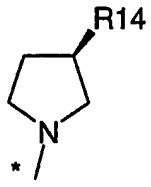

(q)



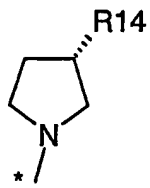

(r)



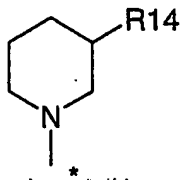

(s)



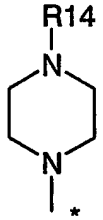

(t)



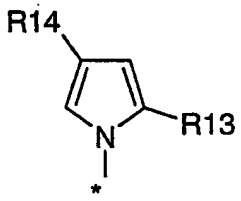

(u)



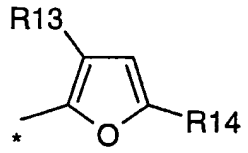

(v)



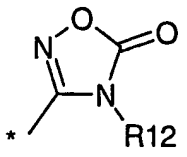

(w)



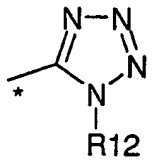

(x)



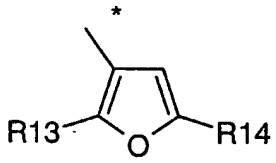

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, -$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, -$C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, -$C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, -$NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, -$S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

12. A compound as recited in Claim 8 wherein:

X is S, O, or $NR^{20}$;or X and the double bond to which it is attached can be 2 hydrogen atoms,

W is S, O, or $NR^{21}$;

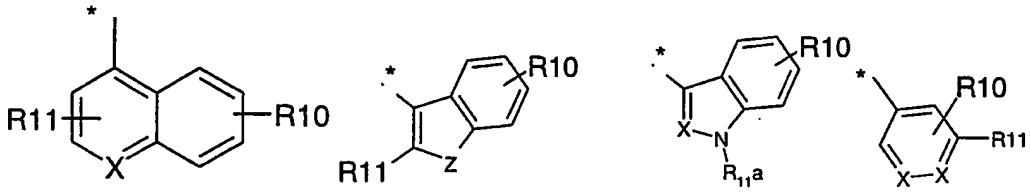
$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^c$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C{=}NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

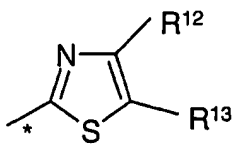
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



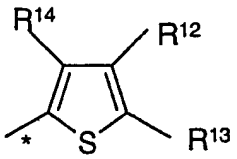

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

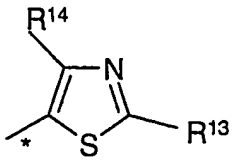
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



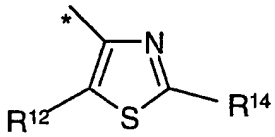
(a)



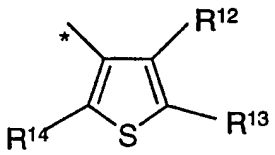
(b)



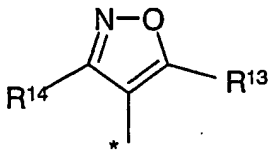
(c)



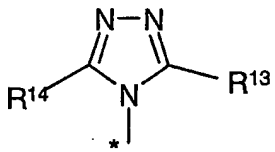
(d)



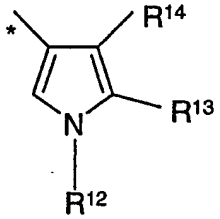
(e)



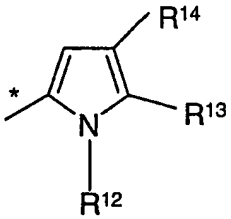
(f)



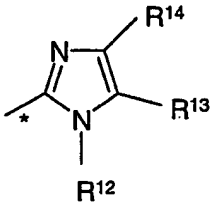
(g)



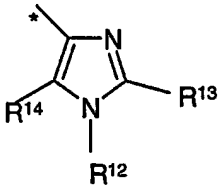
(h)



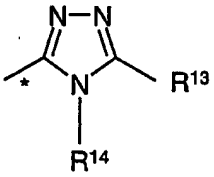
(i)



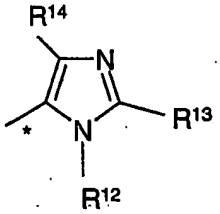
(j)



(k)



(l)



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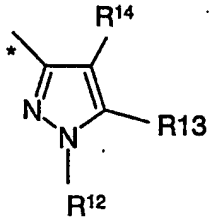

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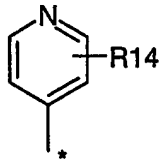

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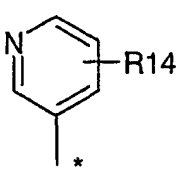
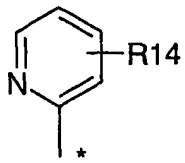
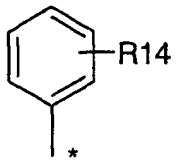


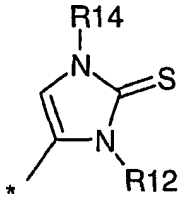

(p)




(q)




(r)

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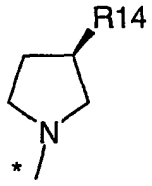
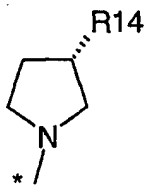
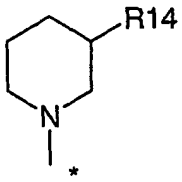


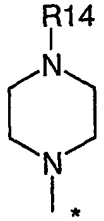

(t)



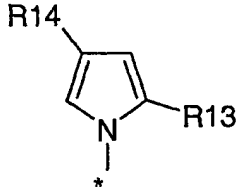

(u)



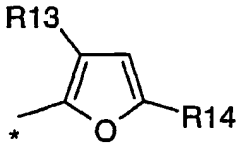

(v)



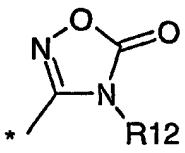

(w)



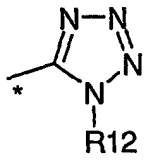

(x)



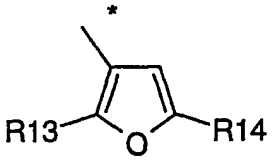

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

13. A compound of formula (II) selected from:

5-{6-amino-2-[(6-chloroquinolin-4-yl)methyl]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-3-methylbutanamide

N,N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-3-methylbutanamide;

N'-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-N,N-dimethylimidoformamide;

5-{2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)(methyl)amino]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]propane-1-sulfonamide;

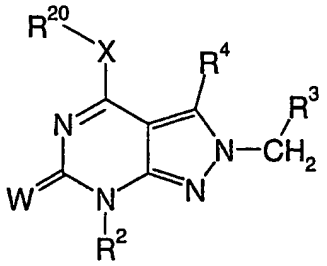
ethyl 2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-ylcarbamate;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-5-methyl-4-oxo-4,5-dihydro-2H-pyrazolo[3,4-d]pyrimidin-6-yl]-N'-ethylurea;

5-[(4*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-5-methyl-4-(methylimino)-4,5-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(4*Z*,6*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-5-methyl-4,6-bis(methylimino)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile.

14. A compound having the structural formula (III):



(III)

wherein,

X is S, O, $NR^{21}$; or $XR^{20}$ is hydrogen;

W is S, O, or $NR^{20}$;

$R^2$ is H, optionally substituted alkyl, optionally substituted alkylcycloalkyl, optionally substituted alkylcycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, or optionally substituted heterocycle;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,$-R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, $-R^5$-$R^5$, $-R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, -

$S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, $-OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^bHet$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{21}$ is, independently at each instance, H, -CN, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$; or

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -C(=O)$NR^aR^a$, -C(=O)$OR^a$, -$NR^aC(=O)R^a$, -OC(=O)$R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, NH($C_{1-4}$ alkyl), N($C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

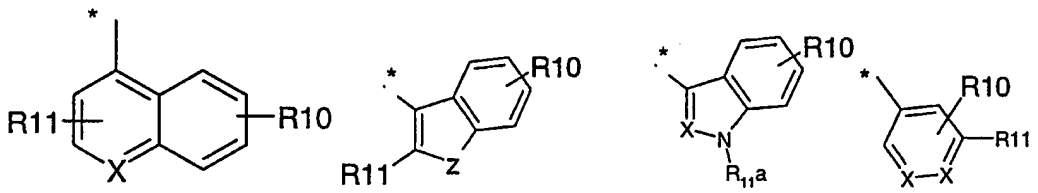
or a pharmaceutically acceptable salt thereof.

15. A compound as recited in Claim 14 wherein:

$R^2$ is –$(CH_2)_{1-3}$cycloalkyl or -$C_{1-12}$alkyl wherein –$(CH_2)_{1-3}$cycloalkyl or -$C_{1-12}$alkyl is optionally substituted with 0, 1, 2 or 3 substituents selected from Het, $S(=O)_nR^c$, halogen, -CN, -$OR^a$, -$NR^aR^a$, -C(=O)$OR^a$, -C(=O)$R^a$, -C(=O)$NR^aR^a$, -OC(=O)$C_{1-4}$alkyl or -$NR^aC(=O)C_{1-4}$alkyl and n is 0, 1 or 2.

16. A compound as recited in Claim 14 wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

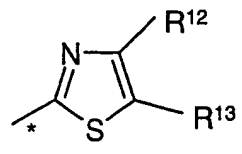



(i) (ii) (iii) (iv)

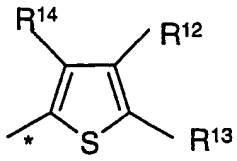
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

17. A compound as recited in Claim 14 wherein:

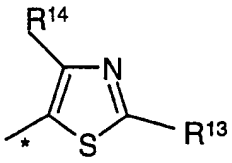
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



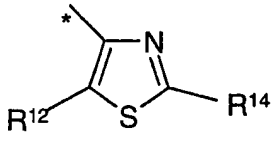
(a)



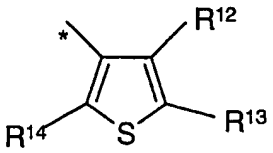
(b)



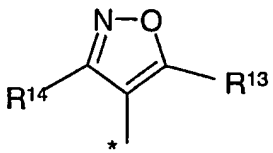
(c)



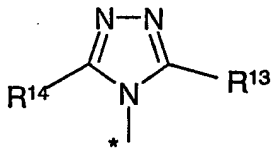
(d)



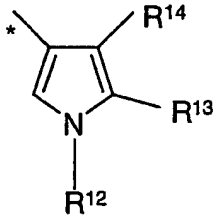
(e)



(f)



(g)



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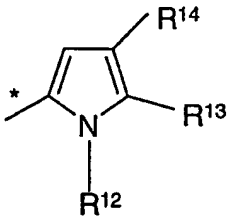

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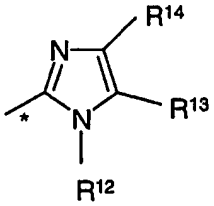

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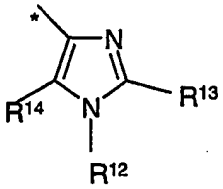

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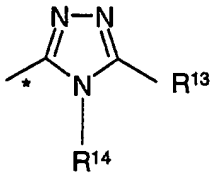

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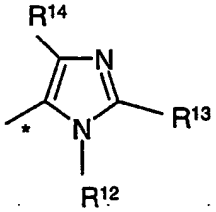

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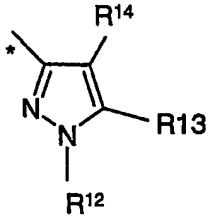

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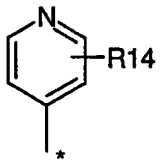

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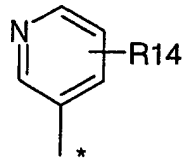


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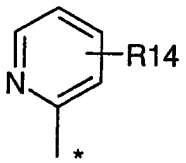


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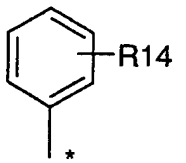


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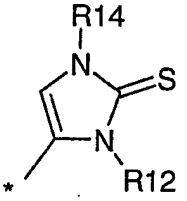


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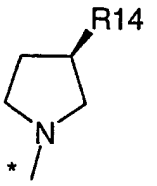


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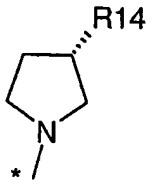


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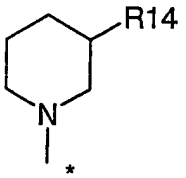


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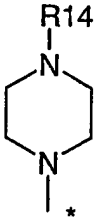


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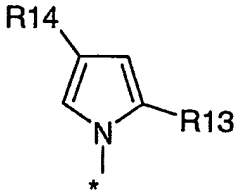


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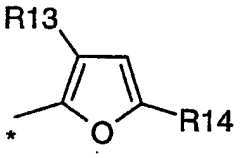


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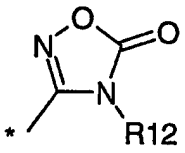


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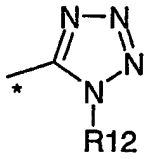
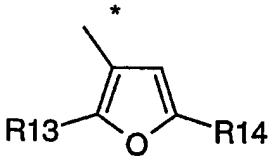



(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

18. A compound as recited in Claim 14 wherein:

X is S, O, or $NR^{21}$;or $XR^{20}$ is hydrogen,

W is S, O, or $NR^{20}$;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

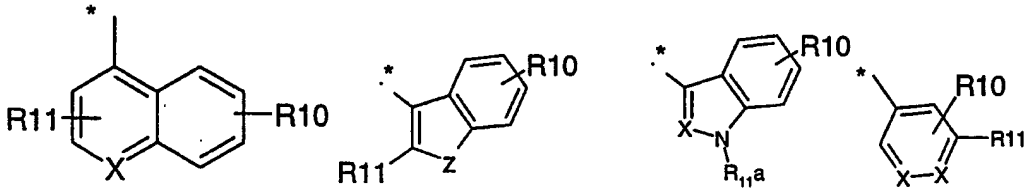
$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

$R^2$ is $-CH_2CH_2CH_3$, $-CH_2$-cyclopropyl, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2F$, $-CH_2$-cyclobutyl, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2$-methylphenyl, $-CH_2$-phenol, $-CH_2$-(3,5-dimethylisoxazol-4-yl), $-CH_2$-S-phenyl, $-CH_2$-phenylcarboxyl, or $-CH_2SCF_3$;

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



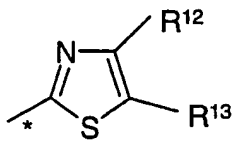

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are

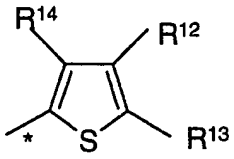
independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:

5



(a)



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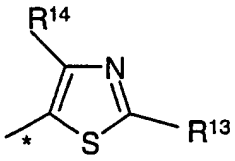
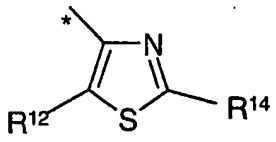
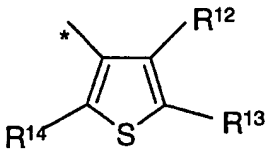


(c)



(d)



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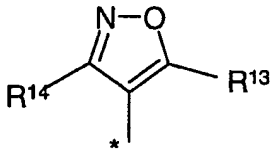

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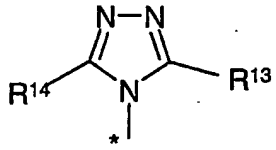

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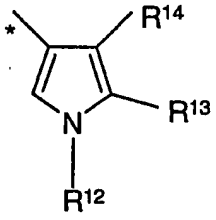

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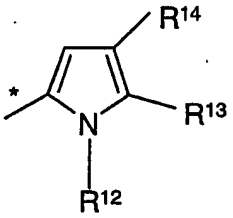
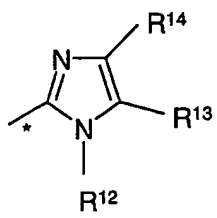


(i)

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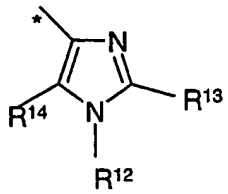


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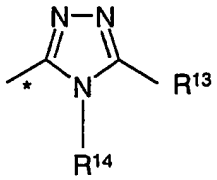


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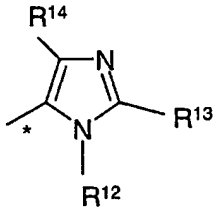


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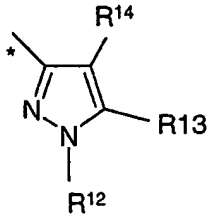


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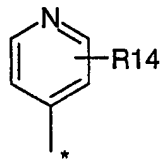


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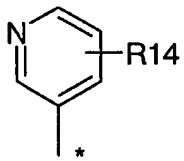


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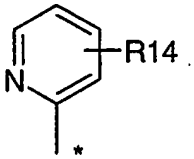


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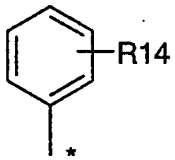


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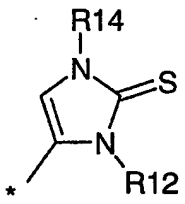


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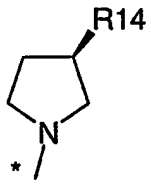


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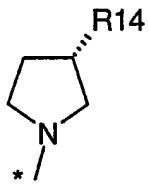


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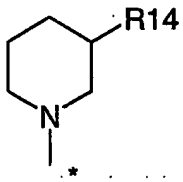


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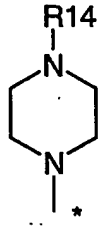


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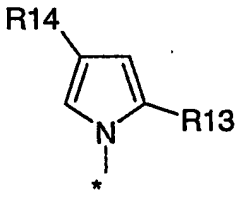
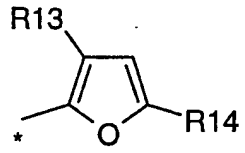
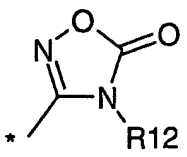



(x)

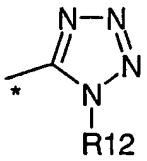
5



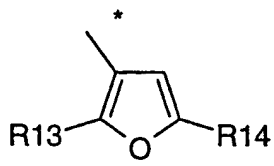

(y)




(z)




(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, $-C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

19. A compound of formula (III) selected from:

4-amino-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

7-isobutyl-4-(methylamino)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

4-(dimethylamino)-7-isobutyl-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

7-isobutyl-4-(4-methylpiperazin-1-yl)-2-(1-naphthylmethyl)-3-pyridin-4-yl-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-3-(1-methyl-1H-pyrrol-2-yl)-2,7-dihydro-6H-pyrazolo[3,4-d]pyrimidin-6-one;

5-{4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-4-(methylamino)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(dimethylamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-isobutyl-6-oxo-4-(propylamino)-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-4-[(2-hydroxyethyl)amino]-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(hydroxyamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(cyclopropylamino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-4-hydrazino-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-4-(2,2-dimethylhydrazino)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

N-[2-[(6-chloroquinolin-4-yl)methyl]-3-(4-cyano-1-methyl-1H-pyrrol-2-yl)-7-isobutyl-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-4-yl]acetamide;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-(methylthio)-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl]-1-methyl-1H-pyrrole-3-carbonitrile;

5-{2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-[(2-hydroxybutyl)amino]-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl}-1-methyl-1H-pyrrole-3-carbonitrile;

5-(2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-{[(2R)-2-hydroxypropyl]amino}-6-oxo-6,7-dihydro-2H-pyrazolo[3,4-d]pyrimidin-3-yl)-1-methyl-1H-pyrrole-3-carbonitrile;

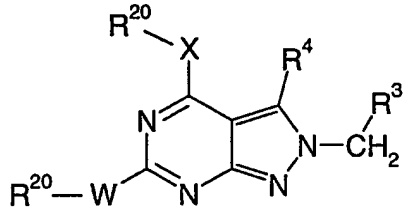
5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-methoxy-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-4-(1*H*-pyrrol-1-yl)-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[(6*Z*)-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-4-(methylamino)-6-(methylimino)-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;

5-[4-amino-2-[(6-chloroquinolin-4-yl)methyl]-7-(cyclopropylmethyl)-6-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile.

20. A compound having the structural formula (IV):



(IV)

wherein,

X is S, O, $NR^{21}$; or $XR^{20}$ is hydrogen;

W is S, O, or $NR^{21}$;

$R^3$ is a monocyclic or bicyclic, saturated or unsaturated, ring system comprising 0, 1, 2 or 3 heteroatoms independently selected from N, O, or S, the ring being substituted by 0, 1, 2 or 3 substituents selected from =O, halogen, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, nitro, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $N=NR^a$, aminocarbonyl, phenyl, benzyl; or $R^3$ is represented by -Het, -Het-Het, $R^5$,-$R^5$-Het, -Het-$R^5$, -Het-O-$R^5$, -$R^5$-$R^5$, -$R^5$-$OR^5$;

$R^4$ is a monocyclic or bicyclic, saturated or unsaturated, ring system, or a vicinal-fused derivative thereof, which may contain from 5 to 12, preferably 5 to 10, ring atoms, 0, 1, 2, 3 or 4 of which are heteroatoms independently selected from N, O, or S, the ring system being substituted by 0, 1, 2 or 3 substituents selected from $B(OH)_2$, vicinal $-OCH_2CH_2O-$, vicinal -$OC_{1-2}$haloalkylO-, vicinal $-OCH_2O-$, vicinal $-CH_2OCH_2O-$, =O, halogen, $-R^bOR^a$, $-SR^a$, $-OR^a$, $C_{1-6}$alkyl, $C_{1-6}$haloalkyl, -CN, $-S(=O)_nR^c$, $-O(CH_2)_mHet$, $-O(CH_2)_mC(=O)Het$, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_mHet$, $-S(CH_2)_mC(=O)Het$, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, -

$S(CH_2)_mOR^a$, $-NR^aR^a$, $-NHC(=O)R^a$, $-NHC(=O)OR^a$, $N=NR^a$, $NO_2$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_nR^a)$, $-C(=O)NR^a(R^bHet)$, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, $-S(=O)_2NR^a(R^bC(=O)OR^a)$, aminocarbonyl, phenyl, benzyl; or $R^4$ is represented by $-(CH_2)_nR^5$-Het, $-(CH_2)_nR^d$, -Het, -Het-Het, $R^5$, $-R^5$-Het, -Het-$R^5$, -Het-$OR^5$, $R^5$-$R^5$, or $-R^5$-$OR^5$; or $R^4$ is represented by $C_{1-6}$alky, $-NC_{1-6}$alkyl, or $-N(C_{1-6}alkyl)_2$ wherein the $C_{1-6}$alkyl, $-NC_{1-6}$alkyl, $-N(C_{1-6}$alkyl) are substituted by 0, 1 or 2 substituents selected from $R^a$, $OR^a$, halogen or phenyl wherein $R^4$ is not $-(CH_2)_zCH_3$, $-(CH_2)_zCH_2OH$, $-(CH_2)_zCO_2H$, or $-(CH_2)_zCO_2C_{1-6}$alkyl wherein z is 1,2,3,4,5, or 6;

$R^5$ is independently at each instance, phenyl substituted by 0, 1, 2, or 3 groups selected from halogen, $C_{1-6}$haloalkyl, $-OC_{1-6}$haloalkyl, $C_{1-6}$alkyl, -CN, nitro, $-OR^a$, $-S(=O)_nR^c$, $-O(CH_2)_m$Het, $-O(CH_2)_mC(=O)$Het, $-O(CH_2)_mC(=O)NR^aR^a$, $-O(CH_2)_mC(=O)OR^a$, $-O(CH_2)_mNR^aR^a$, $-O(CH_2)_mOR^a$, $-S(CH_2)_m$Het, $-S(CH_2)_mC(=O)$Het, $-S(CH_2)_mC(=O)NR^aR^a$, $-S(CH_2)_mC(=O)OR^a$, $-S(CH_2)_mNR^aR^a$, $-S(CH_2)_mOR^a$, $-R^bOR^a$, $-SR^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aOR^a$, $-C(=O)NR^aR^bNR^aR^a$, $-C(=O)NR^aR^bOR^a$, $-C(=O)NR^aR^bS(=O)_nR^a$, $-C(=O)NR^aR^b$Het, $-C(=O)OR^a$, $-OC(=O)R^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-S(=O)_2NR^aR^a$, $-NR^aS(=O)_2R^a$, $-S(=O)_2NR^aR^bC(=O)NR^aR^a$, or $-S(=O)_2NR^aR^bC(=O)OR^a$;

$R^{20}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle, wherein such substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, $(C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{21}$ is, independently at each instance, H, -CN, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$; optionally substituted alkyl, optionally substituted

alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkynyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted amino, optionally substituted heterocycle wherein such substitution is selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido, amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl$)_2$, $C_{1-4}$ alkanoylamino, $(C_{1-4}$ alkanoyl$)_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl$)_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S$(O)_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^c$;

$R^a$ is, independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^b$ is, independently at each instance, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

$R^c$ is $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, phenyl or benzyl;

$R^d$ is phenyl substituted by 0, 1 or 2 groups selected from -CN, halogen, nitro, $C_{1-6}$alkyl, $C_{1-4}$haloalkyl, -OH, -$OR^c$, -$NR^aR^a$, -$S(=O)_nR^c$, -C(=O)$NR^aR^a$, -C(=O)$OR^a$, -$NR^aC(=O)R^a$, -$OC(=O)R^a$, $B(OH)_2$, vicinyl -$OCH_2CH_2O$-, vicinyl -$OC_{1-2}$haloalkylO-, vicinyl -$OCH_2O$-, vicinyl -$CH_2OCH_2O$-, phenyl, benzyl and a 5- or 6-membered ring, saturated or unsaturated heterocycle containing 1, 2, 3 or 4 heteroatoms independently selected from N, O, or S;

$R^e$ is independently at each instance, H, $C_{1-6}$alkyl, -C(=O)$C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1;2,3, or 4 heteroatoms independently selected from N, O or S;

m is 1, 2 or 3;

n is 0, 1 or 2;

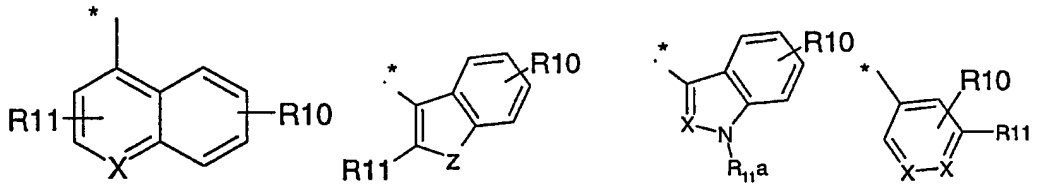
When "optionally substituted" is used, it refers to at least one substituent selected from cyclopropyl, halogen, nitro, cyano, hydroxy, trifluoromethyl, amino, carboxy, carboxamido,

amidino, carbamoyl, mercapto, sulfamoyl, $C_{1-4}$ alkyl, $C_{2-4}$ alkenyl, $C_{2-4}$ alkynyl, $C_{1-4}$ alkoxy, $C_{1-4}$ alkanoyl, $C_{1-4}$ alkanoyloxy, $NH(C_{1-4}$ alkyl), $N(C_{1-4}$ alkyl)$_2$, $C_{1-4}$ alkanoylamino, ($C_{1-4}$ alkanoyl)$_2$amino, N-($C_{1-4}$ alkyl)carbamoyl, N,N-($C_{1-4}$ alkyl)$_2$carbamoyl, ($C_{1-4}$)S, ($C_{1-4}$ alkyl)S(O), ($C_{1-4}$alkyl)S(O)$_2$, ($C_{1-4}$) alkoxycarbonyl, N-($C_{1-4}$ alkyl)sulfamoyl, N,N-$C_{1-4}$ alkyl)sulfamoyl, $C_{1-4}$ alkylsolfonylamino, and heterocyclic

or a pharmaceutically acceptable salt thereof.

21. A compound as recited in Claim 20 wherein:

$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:

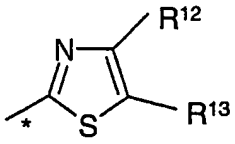



(i) (ii) (iii) (iv)

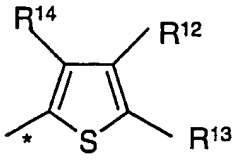
wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

22. A compound as recited in Claim 20 wherein:

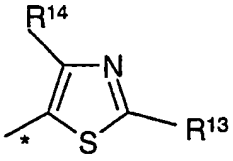
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



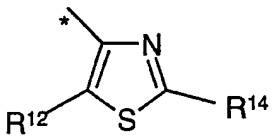
(a)



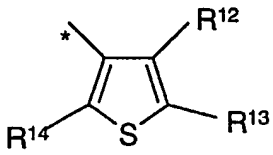
(b)



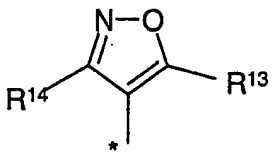
(c)



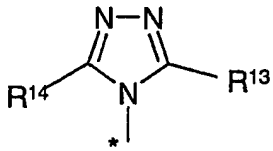
(d)



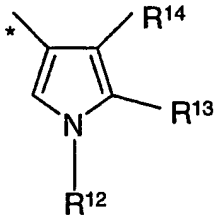
(e)



(f)



(g)



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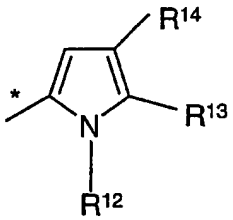
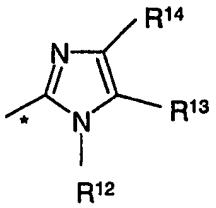


(i)



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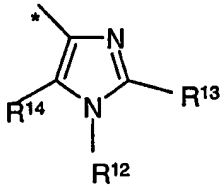
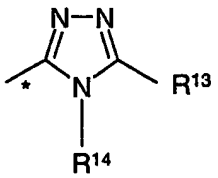


(k)



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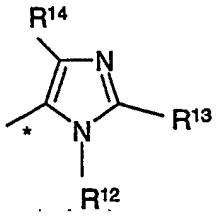

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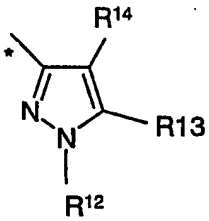

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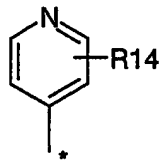

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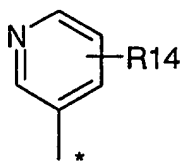


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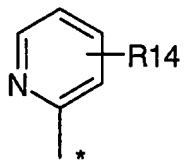


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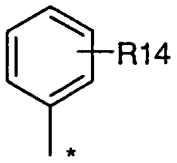


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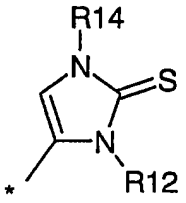


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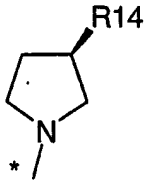


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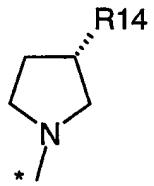


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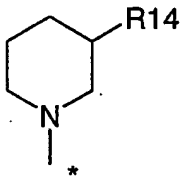


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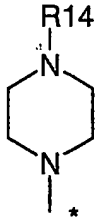


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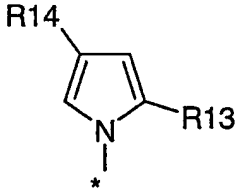


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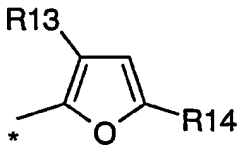


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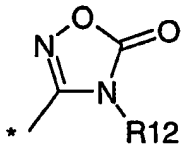


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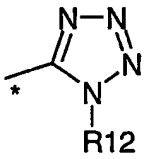
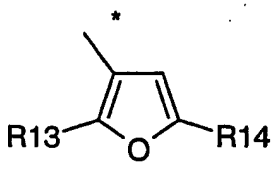



(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, -$C(=O)R^a$, -$C(=O)NR^aR^a$, -$C(=O)NR^aS(=O)_2R^a$, -$C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^b$Het, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

23. A compound as recited in Claim 20 wherein:

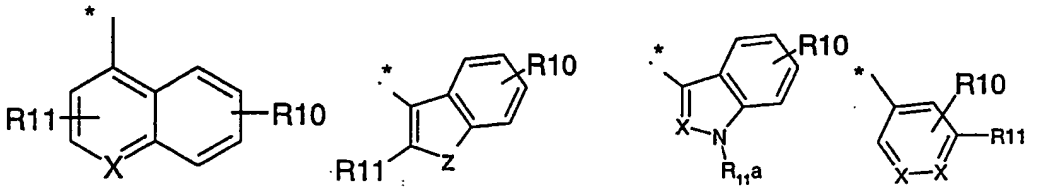
X is S, O, or $NR^{21}$; or X-$R^{20}$ is hydrogen

W is S, O, or $NR^{21}$;

$R^1$ is $CH_3$, $CH_2CH_3$, $CH_2CN$, $CF_3$, $(CH_2)_2OH$, cyclopropyl, isopropyl, $CH_2CCH$, $(CH_2)_2N(CH_2)_2$, $(CH_2)_2N(C=NH)NH_2$, $-CH_2$-2-pyridyl, $-CH_2$-3-pyridyl, $-CH_2$-4-pyridyl, $-(CH_2)_2$-1-imidazolyl, $-(CH_2)_2$-1-pyrazolyl, $-(CH_2)_2$-1-piperidyl, $-(CH_2)_m$-(1-methylpiperidin-4-yl), $-CH_2$-(1-methylpiperidin-3-yl), $-(CH_2)_2$-(morpholin-4-yl),

$R^2$ is $-CH_2CH_2CH_3$, $-CH_2$-cyclopropyl, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2F$, $-CH_2$-cyclobutyl, $-CH_2C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CF_3$, $-CH_2$-methylphenyl, $-CH_2$-phenol, $-CH_2$-(3,5-dimethylisoxazol-4-yl), $-CH_2$-S-phenyl, $-CH_2$-phenylcarboxyl, or $-CH_2SCF_3$;

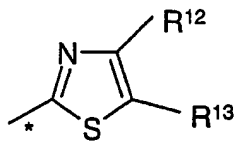
$R^3$ is selected from formulas (i), (ii), (iii) or (iv) set forth below:



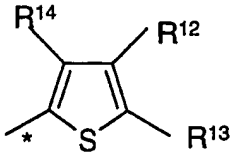

(i) (ii) (iii) (iv)

wherein * is the location where (i) or (ii) or (iii) or (iv) is attached to structural formula (I), and X is C or N; and Z is O or S, wherein $R^{10}$ is at any position on the ring and $R^{10}$ and $R^{11}$ are independently at each instance H, $R^a$, halogen, -CN, nitro, $OR^a$, $CF_3$, $-NR^aR^a$, $-C(=O)OR^a$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-OC(=O)C_{1-4}$alkyl, $-NR^aC(=O)C_{1-4}$alkyl or $-S(=O)_nR^c$; and wherein $R^{11a}$ is $R^a$, $-S(=O)_2NR^aR^a$ or $-S(=O)_nR^c$ and n=1 or 2.

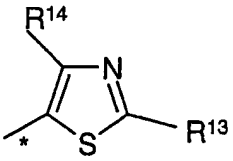
$R^4$ is selected from formulas (a) to (z) or (aa) or (ab) set forth below:



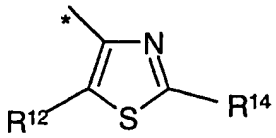
(a)



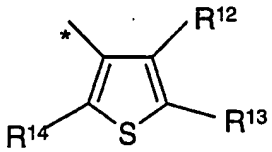
(b)



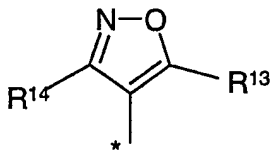
(c)



(d)



(e)



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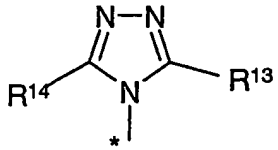
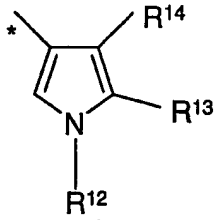


(g)



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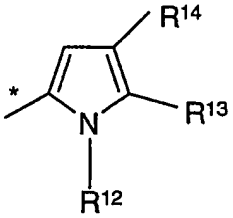
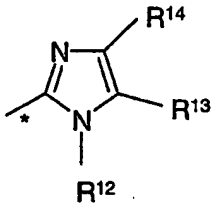
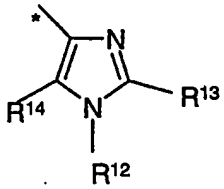


(i)



(j)



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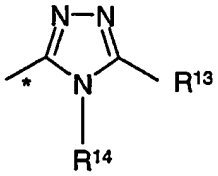

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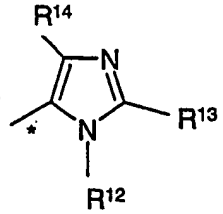

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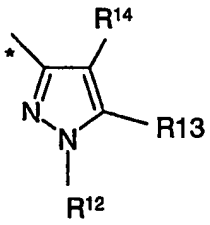

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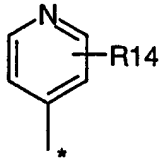

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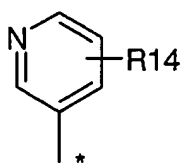


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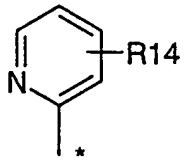


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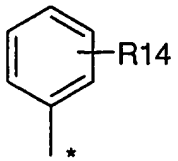


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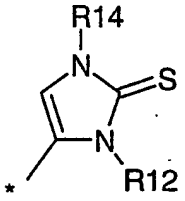


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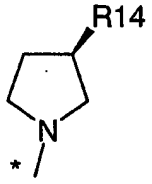


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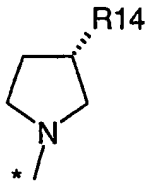


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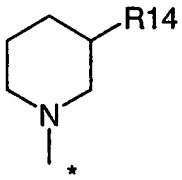


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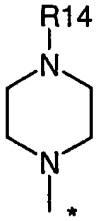


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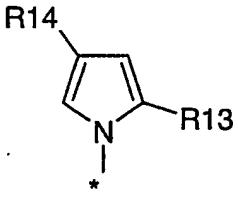


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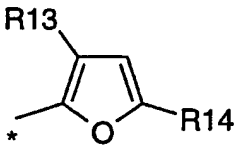


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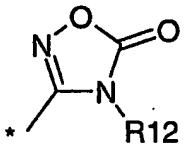


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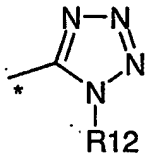
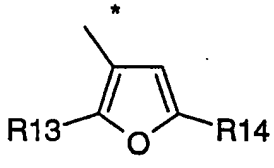



(aa)




(ab)

wherein * is the location wherein $R^4$ is attached to the ring system and wherein wherein $R^{12}$, $R^{13}$ and $R^{14}$ are each independently represented by H, Het, $C_{1-6}$alkyl, -CN, -$NR^aR^a$, -nitro, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)NR^aS(=O)_2R^a$, $-C(=O)NR^a$-Het, -

$C(=O)NR^aNR^aR^a$, $-C(=O)NR^a(R^bNR^aR^a)$, $-C(=O)NR^a(R^bOR^a)$, $-C(=O)NR^a(R^bS(=O)_2R^a)$, $-C(=O)NR^aR^bHet$, $-C(=O)NR^aOR^a$, $-C(=O)R^bNR^aR^a$, $-C(=NOR^a)R^a$, $-C(=NCN)R^a$, $-C(=O)OR^a$, $-C(=O)OR^bNR^aR^a$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)R^a$-$SR^a$, =S, $-NR^aC(=O)R^a$, $-NR^aC(=O)OR^a$, $-NR^aS(=O)_2R^b$, $-C(=NOR^a)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^a$, $-S(=O)_2NR^a(R^bC(=O)NR^aR^a)$, or $-S(=O)_2NR^a(R^bC(=O)OR^a$.

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ is H, -CN, $R^a$, $-OR^a$, $-NR^aR^a$, -Het, $-S(=O)_nR^c$, $-C(=O)R^a$, $-C(=O)NR^aR^a$, $-C(=O)OR^a$, $-NR^aC(=O)R^a$, or $-OC(=O)R^a$;

$R^{20}$ and $R^{21}$ and the N to which they are attached in combination can also form a 3 to 10 member N-linked saturated or unsaturated heterocycle having either 1, or 2 heteroatoms independently selected from N, O, or S wherein the heterocycle is substituted with $R^e$;

$R^c$ is independently at each instance, H, $C_{1-6}$alkyl, $-C(=O)C_{1-4}$alkyl, $C_{1-4}$haloalkyl, phenyl, benzyl, or 5 or 6-memebered ring, saturated or unsaturated heterocycle containing 1,2,3, or 4 heteroatoms independently selected from N, O or S;

24. A compound of formula (IV) selected from:
5-[2-[(6-chloroquinolin-4-yl)methyl]-6-[(cyclopropylmethyl)amino]-4-(methylamino)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]-1-methyl-1*H*-pyrrole-3-carbonitrile;
*N*-{3-(4-acetyl-1-methyl-1*H*-pyrrol-2-yl)-2-[(6-chloroquinolin-4-yl)methyl]-4-methoxy-2*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl}-2-cyclopropylacetamide.

25. A compound according to any one of claims 1 to 24, for use as a medicament.

26. The use of a compound as defined in any one of claims 1 to 24, in the manufacture of a medicament for the treatment or prophylaxis of disorders associated with *H. pylori* infection.

27. A method for the treatment of infections associated with *H. pylori* comprising administering to a host in need of such treatment a therapeutically effective amount of a compound as defined in any one of claims 1 to 24.

28. A method for the prophylaxis treatment of infections associated with *H. pylori* comprising administering to a host in need of such treatment a therapeutically effective amount of a compound as defined in any one of claims 1 to 24.

29. A method for the treatment or prophylaxis of *H. pylori* infection comprising administering a therapeutically effective amount of a compound as defined in any one of claims 1 to 24 or a pharmaceutically acceptable salt as claimed in any one of claims 1 to 24.

30. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 24, together with at least one pharmaceutically acceptable carrier, diluent or excipent.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT SE2003/002033

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 27-29
because they relate to subject matter not required to be searched by this Authority, namely:
see extra sheet

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Box II.1

Claims 27-29 relate to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/Rule 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds/compositions.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/002033

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C07D 487/04, A61K 31/519, A61P 1/04
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C07D, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI DATA, BIOSIS, CHEM.ABS.DATA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | WO 03002567 A1 (ASTRAZENECA AB), 9 January 2003 (09.01.2003) -- | 1-30 |
| A | WO 9006116 A2 (HENNING BERLIN GMBH), 14 June 1990 (14.06.1990) -- | 1-30 |
| A | Arch Microbiol., Volume 168, 1997, George L. Mendz et al, "Purine metabolism and microaerophily of Helicobacter pylori", pages 448-456 -- | 1-30 |

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 9 March 2004 | 10 -03- 2004 |
| Name and mailing address of the ISA/<br>Swedish Patent Office<br>Box 5055, S-102 42 STOCKHOLM<br>Facsimile No. +46 8 666 02 86 | Authorized officer<br>CAROLINA GÓMEZ LAGERLÖF/BS<br>Telephone No. +46 8 782 25 00 |

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT
Information on patent family members

27/02/2004

International application No.
PCT/SE 2003/002033

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| | | | | EP | 1339368 A | 03/09/2003 |
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| WO | 9006116 | A2 | 14/06/1990 | AT | 85522 T | 15/02/1993 |
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| | | | | JP | 4502005 T | 09/04/1992 |
| | | | | US | 5484605 A | 16/01/1996 |